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Endocrinology

The Bulletin *of the*
Association *for the* Study *of*
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November, 1922

INVITATIONS TO RESEARCH IN ENDOCRINOLOGY

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From the Laboratories of Physiology in the Harvard Medical School.

Among the permanent satisfactions in the life of an investigator are the habit of looking forward towards the next steps in the progress of discovery, and an optimistic faith that the progress of discovery is of prime importance for securing control of natural events, especially when these events have a high degree of significance for the welfare of our fellow beings. Such are the central interests of those who are pioneering in the unexplored territory of internal secretions. There is no doubt of the value of more knowledge in this new territory. The endocrine organs play an essential rôle in fundamental processes—in the growth of the body, in the development of the nervous system, in the orderly succession of physiological states resulting in reproduction, in the mobilizing of the forces of the organism for physical struggle, and in the rate and character of the chemical changes occurring in the metabolic overturn. The endocrine organs are commonly referred to as the "controllers" or the "regulators" of these processes. As I have pointed out elsewhere, however, we must not be misled by these terms. In normal existence no organ has a supreme control. It is bound in a web of interrelations which permit it to be influenced in different ways and

which in turn permit it to influence other organs. Indeed, only through the filaments and channels which hold the separate parts together in a unity does each part have any significance. On the basis of these considerations we are justified in seeking methods by which we can control these potent "controllers," by which we can regulate the "regulators."

When there are so many "next steps" to be taken, when what we really know is so slight compared with what we should know, when the problems to be attacked are so evident, as is the case in the endocrine field, it may seem an elaboration of the obvious to consider the work to be done. There is always the possibility, however, that in the course of such a consideration some one may become interested and be stimulated to undertake research. That is the possibility that the investigator, eager to push forward in his labor, always feels justified in exploiting. Accordingly I propose to consider some opportunities for investigation in what seem to me the most important questions at present confronting us.

NERVOUS CONTROL OF INCRETION

A central problem is that of the nervous government of internal secretion. We now have evidence that the adrenal medulla, the liver and the thyroid gland can be stimulated to extra activity by sympathetic impulses. This knowledge at once gives us fresh insight, for such impulses are sent forth under pain, asphyxia and emotional excitement. And we find, in fact, that these conditions, associated with activity of the sympathetic system, are also associated with signs of activity in these glands (1). Adrenin is discharged by the adrenal medulla, sugar and a pressor material are released from the liver, and some substance is given off by the thyroid which speeds up the rate of beat of the denervated heart.

There are other endocrine structures described as having a nerve supply to their cells. Berkley (1894) figured fine nerve filaments ending in knob-like enlargements on the surface of the cells of the anterior lobe of the hypophysis (2). The cells of the parathyroids likewise are said to be well innervated. Both organs have a rich blood supply, such as that found in the adrenal medulla and in the thyroid glands, i. e., they are arranged for quick secretion. Doubtless these nerves have functional im-

portance, but we are entirely unacquainted with their action. The cells of the islands of Langerhans, according to Pensa (3), are surrounded by a basket-work of nerve fibers. These fibers presumably serve some purpose. Attempts to demonstrate any influence of sympathetic stimulation on the blood-sugar level, however, have thus far proved futile. De Corral's (4) observation that vagus stimulation induces a drop in blood sugar offers a valuable suggestion as to the nature of the innervation of the island cells. The work should be repeated, however, and carefully controlled, and if confirmed, the effect should be tested under more nearly physiological conditions by means of vagus reflexes.

A histological study relative to nervous control of internal secretion should include a careful systematic search for nerve filaments distributed to the cells of glands not yet known to be innervated. It is reported that the interstitial cells of the testis are not supplied with nerves (5). Possibly the cells of the adrenal cortex belong with them. If there is a group of endocrine structures of this type we might be able to classify the glands according to the presence or absence of nervous control. The former might exhibit both chemogenic and neurogenic secretion; the latter would be subject solely to chemical or humoral influences, i. e., would be pure chemo-endocrine organs. Definite progress would result, I believe, from such a classification, if it could be justified, for innervation of the endocrine glands probably means, as in the case of other glands, that they can be brought into special service in time of need. Possibly endocrine activities strictly chemogenic in origin are manifested in rhythmically repeated processes as, for example, in the functioning of the ovaries, where a special or extra display would be of no advantage.

DRUG CONTROL OF INCRETION

In relation to nervous and humoral control of the ductless glands is their control by drugs. Here we are only at the beginning of what may prove to be a big advance. About ten years ago, in collaboration with Aub and Binger, I published a brief note presenting evidence that small doses of nicotine would cause secretion from the adrenal medulla (6). This testimony was soon confirmed by Dale (7), and later by Stewart and Rogoff (8).

These last observers have reported that strychnine (9) and physostigmine (10) also call forth an extra discharge of adrenin. Since the effects of these drugs are produced through their influence in rousing sympathetic impulses, the probability is strong that they can be shown to affect also the liver, and the thyroid gland. Mills has reported, indeed, that there are histological changes in the thyroid after exhibition of strychnine, and has stated that morphine and quinine appear to decrease the activity of the gland (11). The effects of these drugs, however, should be tested by physiological methods. An interesting enquiry lies here.

The influence of anesthetics should be further studied. Ten years ago Elliott reported that ether, chloroform and urethane would cause exhaustion of the adrenal medulla, an effect mediated by the splanchnic nerves (12). A number of improvements in methods of determining adrenal secretion have been made in the last decade, and because Elliott's method has been questioned (13), it is desirable that the influence of anesthetics be again studied, not only in relation to adrenal, but also in relation to hepatic and thyroid activity.

Before leaving the subject of the control of endocrine organs by drugs I wish to allude to one very important achievement, which can be placed to the credit of American investigators—the prevention of simple goiter by means of sodium iodide, as recommended by Marine and Kimball (13). This is an admirable illustration of what may be accomplished when carefully established knowledge has bestowed its reward by giving us power to lessen the ills of both man and lower animals.

INFLUENCE OF DIET ON INCRETIONS

Another line of work which seems promising is that concerned with the influence of diet. Although there is physiological opinion that the liberation of glucose from the liver is not a true internal secretion, because no peculiar new substance is evolved by the hepatic cells, nevertheless the process is related historically in a significant degree to the beginnings of our ideas of internal secretion. It was with reference to this process that Claude Bernard, in 1859, first employed the expression "sécrétion interne." The sugar which can be set free from the liver is stored there in the form of glycogen when the carbohydrate sup-

ply is sufficiently abundant to permit. There appears to be a similar storage of protein, according to the observations of Berg (15) and of Stübel (16). They noted that feeding protein food or even amino acids leads to an accumulation of protein material in the liver. Stübel's discovery that this material is discharged by subcutaneous injection of adrenalin further emphasizes the possible relations of diet to internal secretion. Of course, in diabetes we have had for many years evidence that a mild case can be converted into a severe one by feeding carbohydrate food in amounts surpassing the ability of the organism to metabolize it. This appears to be due to an overpowering demand on the islet cells of the pancreas (17). But what this "demand" really is, how the islet cells are brought into action by the taking of food, needs to be determined. Fortunately, the recent highly important work of Banting, Best and Macleod (18), which has resulted in the isolation of a hormone from the pancreas that is capable of promptly reducing the hyperglycemia of diabetes, promises much light and may lead to new information regarding the insular response to carbohydrate feeding.

The influence of diet on other incretory glands is still largely unknown. Watson has reported that the thyroid of the wild rat may be made to lose practically all its colloid by feeding bread and milk (19). Burget confirmed this observation, but had to keep the animals in an unhygienic condition in order to obtain the result. He found, however, that thyroid hyperplasia could be readily produced by a high protein diet (20). Tanberg likewise has noted marked hypertrophy of the thyroid in cats fed for several months exclusively on meat (21). By giving pregnant sows mainly protein food Hart and Steenbock (22) have produced pigs without hair—a condition which, along with thyroid and other disorders, is observed in our western plains where the iodine supply in the food of domestic animals is deficient. In other words, protein feeding appears to make a demand on the thyroid that is equivalent to depriving the gland of necessary iodine. Possibly these observations can be put to use in controlling thyroid disorders. Rosenbloom (23), indeed, has suggested that in the treatment of "hyperthyroidism" a diet with a low iodine and minimum protein content be given. Clinical studies on this point might yield valuable results.

Physiologists have long known that starvation causes a loss

of weight in most of the organs of the body, with the heart and the central nervous system as notable exceptions. Recent researches have revealed that the adrenal glands, the thyroid and perhaps the pituitary body actually become larger during inanition. McCarrison (24) first reported hypertrophy of the adrenals in pigeons deprived of food, an observation soon confirmed by Vincent and Hollenberg. They state that starvation for 15 days doubles the weight of the adrenals of pigeons, and that it produces similar hypertrophy in rats and dogs (25). Soldiers who died in prison camps, where they had been poorly fed, likewise showed this effect, with the enlargement chiefly in the cortex (26). According to Vincent and Hollenberg the adrenin content of the adrenals was at first increased by inanition, but later was greatly reduced. The thyroid glands, though hypertrophied, were almost lacking in colloid (27). Sheep, inadequately fed, have been reported as having thyroids with a much smaller amount of iodine than normal (28). And in advanced inanition there may be marked hydropic degeneration of the gland cells (29).

The effects of deprivation of food may be largely due to absence of certain vitamines. McCarrison's studies on pigeons, guinea pigs, and monkeys have shown that a diet deficient in vitamines will induce enlargement of the adrenal glands and, in the male, of the pituitary as well (30). There is not time to consider these interesting studies in detail. These examples suggest promising opportunities for further valuable work on dietary control of the endocrine organs.

In relation to adrenal enlargement from starvation, the enlargement from feeding thyroid substance may be mentioned (31). In both conditions a mechanism to protect the bodily reserves would be advantageous—some device for reducing the rate of chemical destruction when the food supply is lacking and also when the burning of the supply is being overstimulated. It may be that hypertrophy of the adrenal cortex is related to such a protective service. The suggestion of Shapiro and Marine (32) that in exophthalmic goiter there is a relative functional insufficiency of the suprarenal cortex may have pertinence in this relation. Before we are justified in drawing any definite conclusions, however, these hints must be worked out and the degree of their correspondence to actual fact established.

The origin of the active agents of the internal secretions is a matter of considerable interest. Before much work can be done on this topic, however, we shall have to know more about the chemical composition of the various gland products. In the case of adrenin it happens that we have learned that the chemical structure closely resembles tyrosine. Possibly feeding experiments, in which this one of the amino acids is given in excess or is withheld for some time, would induce corresponding changes in adrenin formation.

SEASONAL VARIATION OF INCRETORY FUNCTIONS

A highly interesting aspect of endocrine function which needs to be systematically examined is the seasonal variation of activity. The most striking illustration of this phenomenon is that afforded by the changes which accompany breeding. The approach of the breeding season in many animals is manifested by a greatly increased activity. Male birds perform strange antics or rapid flights, probably from the operation of some internal impulse (33). Secondary sexual characteristics are developed at this time. "In the spring a livelier iris changes on the burnished dove"—a change doubtless associated with the functioning of the interstitial tissue of the gonads. The stags have fully developed antlers at the time of rut: during that season they are in a state of constant excitement, fighting one another for possession of the hinds. A month or two later, when the excitement and fighting have ceased, the stags once more herd together peaceably, and shortly thereafter the antlers are shed. Since antlers are prematurely shed as a consequence of castration, and thereafter fail to grow, this culminating process, occurring in the red deer in September and October, may properly be regarded as evidence of seasonal recurrence of endocrine activity. Catlin's description of the analogous period, as it used to occur in herds of bisons many years ago, is so vivid that I cannot forbear quoting it:

> "The *running season*, which is in August and September, is the time when they congregate in such masses in some places as literally to blacken the prairies for miles together. It is no uncommon thing at this season, at these gatherings, to see several thousand in a mass, eddying and wheeling about under a cloud of dust, which is raised by the bulls as they are pawing in the dirt or engaged in desperate combats, as they constantly are, plunging and butting at each other in

the most furious manner. In these scenes the males are continually following the females, and the whole mass are in a constant motion; and all bellowing (or 'roaring') in deep and hollow sounds which, mingled together, seem, at the distance of a mile or two, like the noise of distant thunder" (34).

Again we must regard this extraordinary behavior as being determined by a seasonal appearance of endocrine function.

There is evidence that in the lower primates and also in uncivilized man a breeding season exists. Among primitive peoples annual festivals—usually in the spring—were attended by great sexual license, and may have been the outcome of the awakening of powerful impulses at that time. Even in civilized conditions there are some indications of a pairing season. The largest number of births usually falls in the month of February, corresponding to conceptions in May and June. Statistics from Sweden indicate the largest number of conceptions in June, whereas statistics from Greece and Italy point to April and May as the time when they occur most frequently, i. e., the farther south the earlier the period (35). It is remarkable that in spite of the great gaps which separate modern man from the influence of climatic changes—because of clothing and shelter, warm houses and continuous food supply—there should still persist indications of a seasonal periodicity of the reproductive function. Possibly the effects of seasons are to be seen in a more striking degree in cold climates than in warm or tropical regions, and perhaps among rural populations, more exposed to climatic changes than are the city dwellers. Statistical studies of these possibilities might yield very suggestive results.

We have also highly interesting evidence of seasonal variations in the thyroid gland. In 1913, Seidell and Fenger reported that in general there is from two to three times as much iodine in the thyroid glands of cattle, hogs and sheep during the months between June and November as during the months between December and May. The months showing a maximal content were September and October, those with a minimal content were March and April (36). Fenger has more recently confirmed these observations and has shown that the average maximal iodine content is about ten times the minimal quantity for cattle, about seven times for sheep and two and a half times for hogs (37). In this connection a recent experience of my own may be cited. Smith and I had found that massage of the cat's

thyroid gland or stimulation of it by conditions arousing nerve impulses in the cervical sympathetic strand would accelerate the denervated heart. The observations were made chiefly in December. Attempts to repeat the experiments with massage in March and April gave slight or negative results. We are now looking forward to the autumn months with great interest.

Fenger is inclined to attribute the variations chiefly to the effects of temperature, for in cattle and sheep, though not in hogs, the onset of cold weather is followed within a week or two by a noticeable enlargement of the thyroids and a lowering of the iodine percentage. The observation of Mills (38) that rabbits, guinea pigs and cats, though kept on a constant diet, showed signs of increased thyroid activity when subjected to cold, the testimony of Loeb that compensatory hypertrophy of the thyroid of guinea pigs after extirpation of most of the gland is less in the warmer months (May to October) than during the winter (39), and the changes noted by Hart—a decrease of the size of the thyroid and a disappearance of the colloid in mice when kept in a warm atmosphere, with signs of greater activity in cold surroundings (40)—all these experimental results lend support to the conclusion that seasonal variations of temperature may effect to a marked degree the activities of the thyroid gland. On the other hand, Reid Hunt noted striking seasonal changes of thyroid function, in *opposite* directions for guinea pigs and mice, as revealed by his acetonitrile test, when the animals were fed on a fairly uniform diet and kept in the laboratory under fairly constant temperature conditions (41). He is inclined to attribute the annual thyroid rhythm, therefore, to other factors than diet or the annual temperature oscillations.

From the evidence in hand it is clear that there is work of great importance to be done in further examination of the seasonal changes in the gonads and the thyroid, as well as extension of the studies to other glands of internal secretion. We need to know how these changes may affect human cases. It is well known that pregnancy may bring on tetanic spasms in animals with deficient parathyroid tissue. McCarrison has reported that the endemic tetany of child-bearing women in the Chitral and Gilgit valleys of Northern India is practically confined to the spring months (42). Possibly the parathyroids undergo periodic alterations of functional capacity. A workman's tetany

has been described as occurring in parts of Germany and Austria in certain types of industry; it appears usually twice a year, in the spring and in the autumn. Although attempts have been made to explain the malady in terms of chronic ergotism, it is still mysterious. Possibly here also we are concerned with periodic endocrine changes.

If the thyroid and the gonads exhibit waves of seasonal activity, we should expect to find that the bodily processes influenced by them, such as growth and metabolism, would also manifest seasonal waves. Unfortunately the data which would give us insight into these relationships are still quite meager. The recent studies by Porter, on the growth of school children, may be significant of ups and downs in endocrine action. He has found that when the children are weighed month after month the gain in weight between September and January in both boys and girls is approximately four times the gain from February to June. Indeed, practically all the growth occurs in the autumn; and there appears to be almost a standstill during the late winter and early spring months.

So far as metabolism studies are concerned we have very little on which to rest judgments. To provide adequate data, the basal metabolic rate should be determined on the same individuals at regular periods throughout the year. Tests made upon W. W. P. in mid-winter and in mid-summer brought out the fact that his metabolism was considerably faster in the cold season (43). During an Arctic expedition Lindhard determined on himself the carbon dioxide output in half-hour periods under standard conditions. A series of ten experiments which show remarkable consistency was repeated every two or three months. He found that from April to September the standard metabolism was *increased* as compared with the winter months (44). These scattered observations on seasonal differences in growth and metabolism in man, though not concordant, may be very pertinent to our interest in endocrine effects. And they raise many questions. Are there winter conditions of the human thyroid that are different from summer conditions? If this is not the case in persons living protected lives indoors, or residing in warm parts of the country, may it be true of persons exposed to the severity of our northern winters—e. g., teamsters, brakemen and others whose labor changes little during the year. Pos-

sibly necropsy studies, perferably on subjects confined under controllable conditions, as in asylums and penitentiaries, would yield in time significant data. Again there are questions relative to the incidence and exacerbations of disease. For example, what evidence is there as to the influence of warmth and cold on the occurrence of thyroid disease? Would metabolism determinations reveal any effects of temperature and climate on the disturbed processes? These and other questions at once arise from the facts already ascertained.

RELATION OF AGE TO INCRETORY ACTIVITY

Another group of questions center around the relation of endocrine organs to the age period. We know that the metabolic rate is much more rapid in the child than in the adult, and that as middle life slips on towards senility the rate gradually falls. Are these changes associated with corresponding changes in the internal secretions? In old age does the thyroid, which preeminently influences the speed of chemical processes in the body, show signs of lessened activity? Starr regards the dryness of the skin, the brittleness of the nails, and the loss of hair, characteristic of the later years of life, as due to thyroid deficiency, and claims that they may be stopped by taking small amounts of thyroid substance (45).

When we come to the remarkable sequence of events which leads to maturity—the prepubertal increase in height, the development of secondary sexual characteristics, the increase of bodily vigor, the appearance of reproductive elements—remarkable transformations related to changes in the interstitial tissue of the testis, in the thyroid, in the adrenal cortex and in the pituitary body, as well as gradual disappearance of the thymus, we are confronted with a complex of interrelations altogether too involved to be untangled at present. We must rest on the faith that this wonderfully ordered process, starting on schedule time in the life history, after thirteen or fourteen years of quiescence, is automatically arranged to run its course. Some time we shall know, I believe, the successive stages, and be able to help them onward when they are checked.

HEREDITY AND THE INCRETIONS

Related to the influence of both age and season, as conditions affecting endocrine activity, is the inheritance of endocrine

defects. According to Ennis Smith, what he called "fetal athyrosis"—the disorder of domestic animals already mentioned as characterized by lack of hair, by thin brittle hoofs, by low iodine content of the thyroid in the young—occurs in regions where goiter is more or less endemic. It will be recalled that the iodine content of the thyroid in domestic animals is lowest in March and April and highest in September and October. It is very significant that the litters of pigs born in March and April are more frequently affected with the disease than those born in May and June, and that even in quite unfavorable regions the litters born in the fall are usually normal. The symptoms above described are suggestive of a congenital myxedematous state, occurring in the offspring of animals which have had an insufficient iodine supply in the food (46).

Already there is a considerable accumulation of clinical evidence of a similar linkage between a mother suffering from a defective thyroid and her child. McCarrison has concluded from his extensive studies in Northern India that thyroid dysfunction in the mother is the essential factor in the production of cretinism. These are observations which should be extended, not only in relation to cretins, but also in relation to other victims of endocrine disorders. There is suggestive evidence that mongolism occurs in the later years of the mother's reproductive period, and that it, like cretinism, may be due to thyroid deficiency. But again we are in need of more data, carefully gathered and evaluated.

CRITERIA OF ENDOCRINE FUNCTIONS

Perhaps our most urgent need at present is the development of satisfactory tests of endocrine disturbance. To a degree altogether too great we are compelled to judge mild cases by general impressions. At least current literature indicates that diagnoses are made on relatively slight objective signs. If Shelley had "a hyperthyroid face," as has been suggested, it would be well if we could all know just what a hyperthyroid face is. Many years ago Galton suggested the possibility of registering general impressions by means of composite photography (47). It might be an enterprise of much interest to learn whether typical endocrine features could be registered by this means. If

we must depend on appearances, this would seem to be a feasible method of learning the recognizable traits.

We may not have to depend on such uncertain methods, however, for the internal secretions, as chemical agents, may in time be given adequate chemical tests. Meanwhile, we have already the beginnings of fairly satisfactory physical and biological tests. In skillful hands the basal metabolic rate is an excellent measure of thyroid variation from the normal. The test suggested by Goetsch (48), designed to reveal hyperthyroid activity, is criticized because it is positive in cases which do not have other indications of extra thyroid function (49). There is no question of the phenomena observed by Goetsch, but theoretically they may be due not only to hyperthyroidism but also to excessive activity of the sympathetic system and to increased secretion of adrenin into the blood. By properly conducted experiments, based on present control of these three factors, it might be possible to distinguish between them, and thus to refine the procedure. It is conceivable, indeed, that the Goetsch test could be made to apply to two conditions instead of one, and at the same time be more accurate than at present.

ENDOCRINE INTERRELATIONSHIPS

If the finding of objective tests of endocrine disorders is our most urgent task, the untangling of the net of endocrine relations is doubtless our most difficult one. The possibilities of mutual influence are so extensive, the clinical and experimental methods now available are so limited, the difficulties of closely reproducing in lower animals the disturbances seen in man are often so great, that we might well despair of ever solving the riddle. It seems to me, however, that we have certain general principles to go on. First, in the normal organism the orderliness is due to automatically adjusted equilibria. Second, in attempting to learn the operations of the factors concerned in an equilibrium we must consider each one not only by itself, but also in relation to all the others that are engaged in the same service. For example, growth is influenced by the interstitial tissue of the testis, by the anterior lobe of the pituitary and by the thyroid. We should expect, on the basis of what I have suggested, that these three organs normally work in cooperation, and that a disturbance in one would influence both

the process of growth and the relations of the other organs to that process. Possibly by classifying the endocrine glands on the basis of their common effects, their interrelations would prove to be simpler and less mystifying than they now appear and we should have sufficient insight to see where the threads which we have in our hands really lead us.

CONCLUSION

At the outset I spoke of two of the satisfactions in the life of the investigator—the forward look and faith that new knowledge gives new power. I might have added another satisfaction which he enjoys—the use of his imagination. Usually one engaged in research hesitates to mention the ideas he has projected because they so often prove to be futile. And if I may judge from my own experience, a number of the suggestions for new work which I have made above will prove to be futile. They were not made, however, because they represent certainty of results, but because they disclose attractive possibilities of investigation. If perchance anyone is stimulated to set about some task in relation to the problems we have been considering, my purpose would be secured. And if results should come from the effort, there would be especial satisfaction.

It is evident, I think, that there is no more interesting field for research in medicine or biology at present than that of internal secretion. It is a field which calls for both the laboratory worker and the clinician. One needs only to mention Addison and Graves, von Mehring, Kocher and Marie to prove that most of the early advances in endocrinology were due to clinical studies. The clinic presents types of disorder which the laboratory does not know. But the laboratory frequently offers the advantage of much simplified and more controllable conditions. In the studies which I have suggested, however, there are opportunities not only for clinicians and experimenters, but for histologists, and for statistical experts, for observers skilled in photography, and for biochemists. There is plenty for all of us to do. In a co-operative spirit we must push onward, continuing to apply the well-tried methods of critical observation, limited inference, and discriminating test, with the assurance that only thus shall we firmly establish the truth.

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THE GLANDULAR STATUS OF BROWN MULTILOCULAR ADIPOSE TISSUE

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This review seems justified by the fact that the brownish-colored and gland-like multilocular adipose tissue found in many mammals has repeatedly been considered to be an incretory gland and by the further fact that recently it has been suggested that it may be of importance in connection with deficiency diseases.

NAMES BY WHICH IT HAS BEEN KNOWN

While this multilocular adipose tissue is most often termed the *hibernating gland* (Barkow), it is met with in the literature under a variety of other names—*adipose gland* (Rudolphi), *oil gland* (Jones), *brown fat* (Hammar), *lipoid* or *cholesterin gland* (Cramer), *organ of hibernation* (von Hansemann), and *hibernating mass* (Vignes). A circumscribed fat mass in human foetuses in the dorso-cervical and interscapular regions, which some consider a homologous structure, has been called the *interscapular gland* by Hatai. As will be evident from the following discussion, there is very little and frequently no justification for many of these terms. The safest designation at the present time would seem to be *multilocular adipose tissue.*

GENERAL STRUCTURE AND COMPOSITION

In gross appearance it resembles very much a lobulated gland such as a salivary gland. Its fatty character is not suspected till examined microscopically. It consists of densely packed cells, 25 to 30 micra in diameter, whose cytoplasm is greatly distended with fat globules. These cells are bound together to a large extent by an unusually close plexus of capillaries. It differs from ordinary adipose tissue in that the essential cells are multilocular, much richer in granular cytoplasm and smaller in size. The nucleus remains spherical and, while frequently very eccentric in position, is never flattened

against the margin. Carlier and Evans (1903) could obtain only 40 per cent of fat by weight from this tissue in the case of the hedgehog as compared with a yield of 90 per cent often obtainable from ordinary adipose tissue. As might be expected, they found as high as 15 to 16 per cent protein in the hibernating gland. Shattock (1909) reports that the iodine value of the fat differs in the two types of adipose tissue. According to Vignes (1913) the fatty material in the hibernating gland of the rat is composed largely of a substance closely related to lecithin, probably jecorin. Cramer (1920) also stresses the presence of considerable cholesterin and other lipoids, and yet Carlier and Evans (1903) found in the hedgehog that nine-tenths of the fat in the hibernating gland was olein, the remainder being sterin with a trace of palmitin, lecithin and pigment. The greater amount of pigment in the multilocular fat may play some rôle in preserving the unsaturation equilibrium of the fats, as suggested by Currie (1922). Although Carlier and Evans also made determinations on the mineral content and the solubility of the fat, the chemistry of this tissue is too meager to warrant any general conclusions.

In hibernating animals the amount of fat present and hence the size of the cells and the whole structure vary with the season of the year. It is maximum just before the onset of dormancy. It decreases slowly during winter-sleep and then more rapidly in the spring as the animal becomes active. The whole tissue is thus reduced to about one-fourth of its former bulk. It also becomes much darker in color. The cells decrease from 30 micra in diameter to 10 micra. In this reduced condition the cells resemble epithelial cells with an abundant granular cytoplasm in which is an occasional fat globule. There is no evidence that any cells revert to fixed connective tissue cells. The nucleus remains spherical in shape and unchanged in size. As summer advances the cells become filled with fat again, the tissue becomes lighter in color, and returns to its former size.

While nerves have been described in the organ, especially by Carlier (1893), no nerve supply to the essential cells has been positively demonstrated. (For further details the reader is referred to a forthcoming publication on the hibernating gland to appear in the Journal of Morphology, Philadelphia.)

LOCATION AND DISTRIBUTION

Usually there is a large mass of this tissue in the superior mediastinum, about the thymus. Numerous small masses extend upward along the large vessels of the neck and in the intermuscular septa of the cervical region. By means of slender prolongations dorsal to the clavicle, the cervical portion is frequently continuous with a prominent lobe in each axillary fossa. These latter lobes may represent one-half of the entire organ. A pair of lobes is often found between the scapulae and extending forward between the dorsal muscles of the neck. From the mediastinal mass there are slender caudal extensions along each sympathetic chain, aorta, and mammary arteries. In some animals it may extend into the abdominal cavity and form two prominent perirenal lobes. Less frequently isolated masses are found lower down along the aorta and its main branches as far as the inguinal region.

Examination of the literature reveals the fact that it has been found in about 47 species (5 insectivora, 9 chiroptera, 33 rodentia), with some uncertainty in several more species. Since most of them are hibernating animals, the association of this structure with winter-sleep has been repeatedly made; but there is a large number of species (rats, mice, rabbits, etc.) that possess this structure and yet do not hibernate. On the other hand, the organ is not found in some mammals that do hibernate (e. g., European badger).

The locations most often mentioned are the thoracic and cervical. Next in order come the axillary and interscapular. It is still less often indicated in the renal, while the inguinal is least often the site.

ITS HOMOLOGY IN MAN

Rather distinct circumscribed fat masses in the posterior triangle of the neck and axillary and interscapular regions have been described in some detail by Merkel (1899), Charpy (1901), Hatai (1902), Bonnot (1908) and Shattock (1909). Hatai, Bonnot and Shattock consider these to be probably homologous to the hibernating gland of lower forms. Shattock believes that the fatty swellings in the neck and axilla of cretins are the same structures as the hibernating gland which he found in these locations in the hedgehog. These fatty masses in thyroid dis-

orders had been noted previous to this by T. B. Curling (1850) and again by H. Fagge (1871). Cramer (1920) stresses the glandular character of the perirenal fat, which, in the human embryo, appears to him to be essentially like the hibernating gland. But the literature does not present convincing proof of the similarity in structure between these fat masses and the typical hibernating gland. There is also some negative evidence. Berg (1910), who made an extensive examination of human material, Batty Shaw (1902) and Auerbach (1902) were unable to see anything in man that resembled the brown fat of animals.

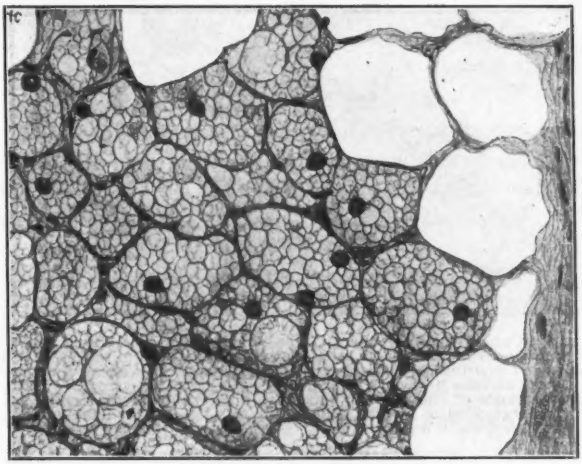

Fig. 1. Camera lucida drawing of multilocular fat cells and a few ordinary adipose tissue cells from the perirenal fat of a normal newborn child. Formalin fixation; celloidin; hematoxylin and eosin. X 400. By comparing this figure with Fig. 2 the similarity in structure between these multilocular fat cells and the essential cells of the so-called hibernating gland of animals is clearly evident.

In spite of the above negations, there are occasionally in the perirenal fat of newborn and very young children cells, as shown in Figure 1, which are in all structural details essentially the same as the typical hibernating gland cells (Fig. 2). Just how often and how widespread such multilocular fat cells may be found in man no one can say for lack of sufficiently extensive examination of human material. The cells here shown in Figure 1 are not developmental stages of ordinary fat, for in the latter case the nucleus is early crowded and flattened against

the cell margin and the droplets coalesce into a larger and larger globule which fills most of the cell long before it reaches the size of those illustrated here. The relatively large amount of cytoplasm is also atypical of ordinary developing adipose tissue. Then, too, no intermediate stages are clearly seen.

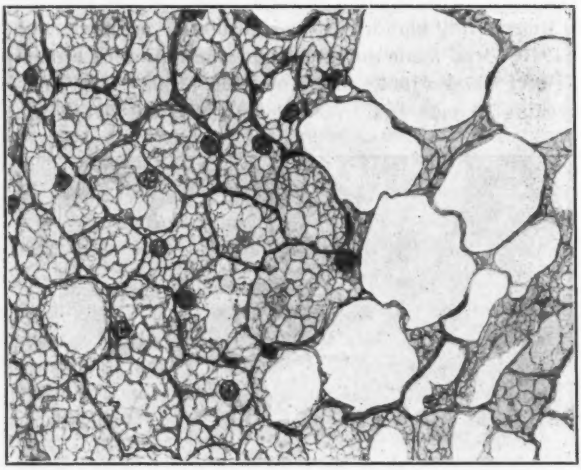

Fig. 2. Camera lucida drawing of the brown fat or hibernating gland cells and a few ordinary adipose tissue cells from the common white rat. The relative abundance and multilocular character of the cytoplasm as well as the spherical shape of the nucleus in hibernating gland cells are well contrasted with the general appearance of the adjacent cells of ordinary adipose tissue. Except for greater shrinkage (due to paraffin embedding) this figure is strikingly similar to Fig. 1, which is from a human subject.

DEVELOPMENT

Carlier (1893) describes these hibernating gland cells in the hedgehog as coming from small round granular connective tissue cells, similar to those that give origin to ordinary fat cells. Hammar (1895) found the anlage of the interscapular lobe in the rat first to differentiate from the mesenchyme in embryos 1.2 cm. in length; but fat droplets did not appear till the latter part of intrauterine life, when it accumulated rapidly. He was unable by feeding rats for three months on a diet rich in fat to change these cells into ordinary adipose cells. There always remained the wide cytoplasmic border. Von Hansemann, who also utilized the rat, found the first trace of these multilocular fat cells in foetuses 1.6 cm. in length in both the dorsal region of the neck

and the axilla. Later it appeared in the neighborhood of the thymus. The cells first appear as large polygonal cells of connective tissue origin. Large blood vessels are associated with these cells before they have differentiated. Both the place of development and the histogenesis, he claims, distinguish this brown glandular fat from ordinary adipose tissue. Bonnot (1908) described the "interscapular gland" in human subjects as arising from the walls of the primitive jugular vein. The tissue which forms in this region differentiates into lymphoid tissue and fatty lobules. The lymphoid tissue in turn develops into lymph nodes and hemolymph nodes. There seems to be no justification, however, for considering the lymph nodes as part of this fatty structure.

FUNCTIONAL SIGNIFICANCE

This gland-like adipose tissue was first mentioned by Velsch in 1670. He thought it was of a lymphatic nature and functionally related to the thymus. The next three writers on the subject (Harder, 1686; Scheuczer, 1727; Buffon, 1749) make no comment on its function. Sulzer (1774) spoke of it as a gland; Pallas (1778), Meckel (1806, 1815), Mangili (1807), Prunelle (1811), and Tiedemann (1815) considered it a part of the thymus.

It was Ludwig Jacobson who, in 1817, first clearly showed that it is a distinct structure and not a part of the thymus. He demonstrated that in marmots, hedgehogs and bats the thymus undergoes the usual involution and in its place develops a fatty tissue which varies in size with the season of the year. This work was repeated by Haugstedt (1831), who fully corroborated the findings of Jacobson. Rudolphi (1830) and Wagner (1835) similarly considered it as only a modified form of adipose tissue; but Burdach (1830), Simon (1845) and Jones (1852) adhered to the old notion that it was a persistent thymus, although Simon recognized that it may become changed to a mass of fat cells.

Barkow (1846) was the first to call it the hibernating gland. Although he recognized that it was a separate organ from the thymus, he considered that it belonged with the ductless glands such as the thymus, thyroid, etc. That it is a separate structure from the thymus, but still a ductless gland probably of the haemopoietic series, was also the belief of Ecker (1853), Valen-

tine (1857, 1859), Leydig (1857), Friedleben (1858), Vogt and Yung (1894) and Wiedersheim (as late as 1907).

Stannius (1853) had the peculiar notion that the sympathetic nervous system developed from its interior.

Beginning with Hirsel and Frey in 1863, the hibernating gland has in general been regarded as a variety of adipose tissue probably serving merely as a source of food during winter-sleep. From histological studies, Hirsel and Frey decided that there is no similarity between this fatty tissue and lymph- or blood-forming organs in general and the thymus in particular, although their idea of the finer structure was entirely erroneous. Sharing very much this same idea of its functional significance are Owen (1868), Fleischel (1869), Afanassiew (1877), Ehrmann (1883), Poljakoff (1888), Carlier (1893), Hammar (1895), Dubois (1896), von Hansemann (1902), Auerbach (1902) and Polimanti (1912). Polimanti suggests that it may also act as a protective cushion enveloping the thorax and thus guarding the internal organs from the external temperature.

Its importance as a special source of food for the hibernating period has, however, been greatly overestimated, at least as far as the amount of material that it yields is concerned, as is evident especially from the figures given by Valentine (1857, 1859). This investigator found that the hibernating gland of the European marmot, while giving up nearly 70 per cent of its weight as food during winter-sleep, represents, to begin with, only 1.33 per cent of the total body weight. Calculations from his figures show that ordinary adipose tissue contributed 20 times as much material during the same time and skeletal muscle 8 times as much and the liver 2 times as much as the hibernating gland. Since other tissues also yield food material it follows that less than one-thirtieth of the consumed body tissues came from the hibernating gland. Carlier (1893) gives somewhat higher figures for the hedgehog, in which the structure represents about 3 per cent of the body weight before hibernation and decreases during dormancy to about 1 per cent.

A number of other investigators (Aeby, 1875; Harvath, 1878, and Ballowitz, 1891) of this period do not commit themselves on the physiological phase of the question.

Although the notion that the hibernating gland is a persistent thymus and the later idea that it is a separate organ but

still of the haemopoietic series were discarded, the theory that it is a gland of some sort persisted. Thus Malesani (1902) was struck with its glandular appearance and considered it to be a ductless gland which was of great importance during hibernation. Shattock (1909), because of the discrete droplets of lipoid which its cells contain, thinks it is allied to the ductless gland, and since it does not behave like ordinary adipose tissue (being spared during the major portion of the dormant period) it is physiologically as well as histologically specialized. Salmon (1910, 1916) argues that it is the only organ that is active during winter-sleep and functions as a true endocrine organ by inhibiting all other glands of internal secretion.

Vignes (1913), from the experiments reviewed in the next section of this paper, concluded that the organ may be considered an economizer of proteins by insuring the utilization of reserved carbohydrates and fats first. This suggestion is interesting in connection with more recent work on the rôle of ordinary fats in the utilization of proteins by diminishing their toxicity and increasing their availability, as argued by Maignon (1921).

Finally Cramer (1920) lays stress upon the fact that the fatty material is rich in cholesterin compounds and other lipoids and that this lipoid is retained during ordinary starvation, but is used up in animals dying for lack of accessory food factors. He suggests that the lipoid has been used up to supply vitamines. From the great similarity in the reaction to polarized light between the suprarenal cortex and this multilocular fat, he assumes that there is also great similarity in composition.

EXTIRPATION EXPERIMENTS

Apparently the first extirpation experiments on record in connection with this multilocular fat tissue are those by Dubois (1896), who first merely exposed the structure in the marmot to see the effects of the necessary preliminary operative procedure. On the following day as much of the tissue as possible was removed. Two of the animals lived two or three days and during this time they exhibited no difficulty in warming up rapidly after torpor.

Auerbach (1902) extirpated the dorsal part of the hibernating gland in a rat. The animal lived two months. There was no regeneration of the lost tissue, its place being occupied by ordinary adipose tissue.

As the results of an extensive series of extirpation experiments in connection with the utilization of extracts of the hibernating gland on white rats and mice, Vignes (1913) found that while most of the rats survived the removal of a large part of the organ (it is improbable that complete removal could be achieved) they lost weight and finally died. Only two lived more than three months. One lived four and one-half months. In the mouse, in which the operation is more difficult, the animals survived indefinitely, although there was an initial loss of weight. The rats operated upon had an increased resistance to adrenalin and cobra venom and a lessened resistance to chloroform. He also found that the extract of this fatty tissue increased the toxic power of tetanus toxin. The organ also apparently modified enzyme action for its extirpation diminished the quantity of lipase in the serum of the rats. It contained a lipase which acted on monobutyrin. The amyloptic power of the serum of the experimental rats was diminished; but extracts of the organ did not act on starch. The extract had an antitryptic power since it inhibited the action of trypsin. Vignes suggests that further studies on this organ would increase our understanding of the rôle of the phosphatides in metabolism. His conclusions have already been stated.

CONCLUSIONS

The brown multilocular adipose tissue, most commonly termed the hibernating gland, but known also by a variety of other terms, seems to be found mostly in rodents, but also in a few species of insectivora and chiroptera. A few similar cells are found occasionally in the perirenal fat of young children and newborn, but certainly there is no good evidence that the masses of fatty tissue described in other regions of the human body should be considered homologous to the hibernating gland of animals. It is not confined to hibernating mammals, nor is it present in all mammals that pass the winter largely in a dormant condition.

It is clearly evident that no one has gone extensively enough into the physiological significance of this brown multilocular adipose tissue to justify its classification as a gland. The granular character of the cytoplasm, the presence of numerous discrete fatty globules and other structural features of this tissue are not sufficient criteria by which to judge its glandular prop-

erties. The prevailing opinion during the past 50 or 60 years has been that it is merely one type of adipose tissue. The best designation for this tissue at the present time would seem to be multilocular adipose tissue.

Its importance as a special source of food for the hibernating period has been overestimated, at least as far as bulk is concerned, yielding as it does only about one-thirtieth of the body tissues consumed in the case of the common European marmot (a slightly higher yield in the American marmot is indicated by figures to be published by the writer in the Journal of Morphology), and about one-fifteenth in the case of the hedgehog.

Extirpation experiments are of little value on account of the extensive distribution of the tissue. The effects of its extracts have been investigated practically by only a single worker (Vignes), who believes he has evidence from enzyme action that it functions as a protein sparer during winter sleep. The latest theory, that it may be a special source of vitamines, is based on such meager data that it need not be taken seriously.

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THE PRESENT POSITION OF TESTICLE TRANSPLANTATION IN SURGICAL PRACTICE: A PRELIMINARY REPORT OF A NEW METHOD

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Much notoriety has recently been given in the lay press to the operation of testicular transplantation. This raises the question of the scientific aspect of the operation in general, hence it is desirable that the medical profession at large should have clear ideas as to its present status and what may be expected from it.

There are but very few cases of human testicular transplantation on record which have been followed by any durable degree of success. In fewer cases still has any scientific histological proof of the "taking" and vascularization of such a graft been given to substantiate claims that the graft was not resorbed. The value of such surgery must lie in the fact that a graft of this kind is able to live and function, and any method of transplantation must in the end be judged by this criterion. In the only case of human transplant reported by Lespinasse in 1913 (3) no such histologic proof was given, although it is stated that, clinically, sexual potency continued after the operation. A thorough search of the literature fails to disclose any other work done on human transplantation by Lespinasse.

Having for some years past been engaged in extensive experimental and clinical work connected with this question, I desire to bring its actual clinical status to notice, and to make a preliminary report on some of the results obtained.

A study of the extensive literature of this question since the first personal experiments of Brown-Séquard (1) shows that the testicle has a double secretion; that of the sperm cells proper, or seminiferous tubuli; and that of the interstitial glandular substance. The secretion of the seminiferous tubuli is concerned alone with fecundation; the interstitial glandular secretion has been clearly proved by a multitude of investigators to

be a hormone acting on the general system. This is a male sexual hormone, acting as a sex stimulant, and responsible for the development and maintenance of sex characters and desire.

The physiological findings naturally led to the investigation of methods having for their object the induction of the incretion in individuals in which it was deficient. The best known of these methods is that of testicular grafting.

Fig. 1. Photomicrograph. Transplant of testis of higher ape into man. Author's technique. Magnification 60 diameters. Observe regression of tubuli seminiferi, proliferation of interstitium and vascularization. Removed four months after transplantation.

By numerous animal experiments it was established that either homo- or hetero-plastic grafting of testicles is possible in animals; that sometimes these grafts "took" and at other times they did not, the difference in results suggesting either a faulty technique or that some racial or specific incongruity rendered the "taking" of a heteroplastic graft impossible. The technical difficulties might be ascribed to difficulty of obtaining vasculariza-

tion in the transplanted tissue due to implantation in an unsuitable region or to an unsuitable method or to both.

The homo- and hetero-graft experiments in animals, supplemented by histological findings, reported in 1919 by Professor Serge Voronoff (2) of Paris (with whom it has been my privilege to collaborate for some years) undoubtedly gave the most brilliant results and proved that transplantation of animal testicular tissue from young to old animals of the same species was followed by viability and could be followed by clinically demonstrable renewal of physical and sexual vigor and sexual impulse which had become lost.

Although various clinical attempts have been made to transplant testicles from man to man the operation can be said to have been only partially successful. In many cases the graft was expelled after a short time and in others it became absorbed after a greater or less interval. It has been generally believed that in the cases where a graft has been retained that it exerted a hormonic influence and that physical well-being and sexual potency was for a while restored. In but few cases, however, was the actual "taking" of the graft verified by histological findings.

From the study of the literature and especially after visiting the clinics of Voronoff in Europe, I was convinced that the operation of testicular transplantation could be made a practical surgical procedure.

The difficulty of vascularization could, I believe, be met by a suitable site and method of implanting the graft. The great difficulty, however, of obtaining perfectly suitable material was not one easily solved, as for obvious reasons human testicular material is difficult to obtain, and is not always likely to be free from disease and suitable for transplanting.

By a series of experimental investigations I devised a method of transplantation which I call the "lantern" technique which has given perfectly satisfactory results as regards the "taking" and rapid vascularization of testicular grafts. I have also succeeded in successfully transplanting the testicles of higher apes to man and have obtained results which are in every way analagous to those obtained in transplantation of human testicles.

Moreover, these transplants of the higher apes have been removed after several months and proved histologically to be in full activity and vascularized. This is the first time that successful transplantation from ape to man has been verified by histological proof.

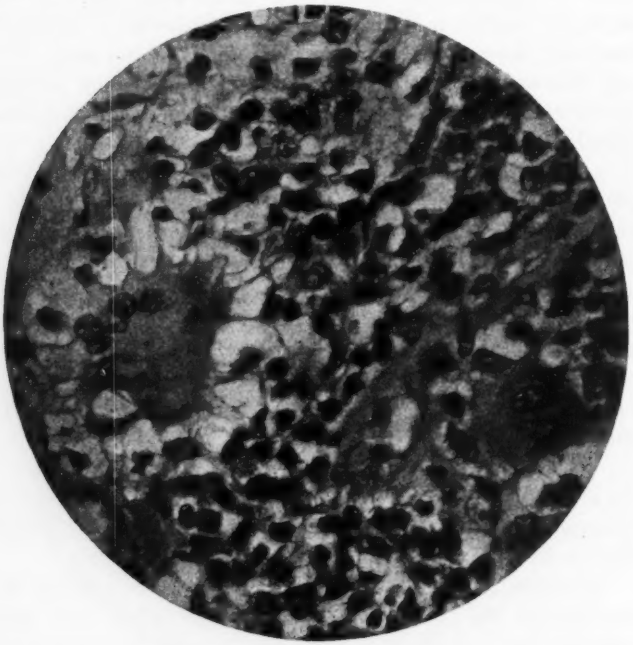

Fig. 2. Same as Fig. 1. Magnification 560 diameters. Observe what appear to be Leydig cells, giant cells and abundance of cell life in well nourished area.

The accompanying illustration is a reproduction of the histological appearance of a section from such a graft which was removed four months after implantation. It shows regression of the seminiferous tubules, proliferation of the interstitial elements of the testicle and vascularization of the graft.

I have done a great many transplantations from the higher apes to human subjects and in the cases where I have employed the improved technique almost invariably excellent results have been obtained.

The full details of my surgical technique and clinical findings will be published later in a more complete report.

SUMMARY

A new technique has been devised whereby it has proved possible to transplant testes from man to man or from higher ape to man and secure persistence of the graft with consequent clinical improvement of symptoms due to gonadal deficiency. Two photomicrographs are reproduced, showing persistence of graft.

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THE STEINACH OPERATION: REPORT OF 22 CASES WITH ENDOCRINE INTERPRETATION

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The ligation of the ductus deferens combined with vasectomy has become now generally known as the "Steinach operation." By its effects, I am inclined to designate it as "endocrine surgery." I shall assume that the theory on which Steinach based his practice is fairly well known, and discuss it only very briefly, referring to my other publications for more detailed information.†

In the 22 cases herewith presented unilateral ligation under local anaesthesia was the rule. The vas was carefully isolated and separated from all accompanying structures for a distance of about 2 cm. Two heavy silk ligatures were placed around the vas, about 2 cm. apart. The one nearer to the testicle was reinforced by a fine silk ligature in order to use it later for sewing the lower stump into the tissue near the upper corner of the wound, for the purpose of suspension. Before this was done, a short piece of the vas between the heavy ligatures was resected. The tunica vaginalis and the skin were closed with catgut. The principle of the procedure is to close the vas, prevent re-communication of the stumps, and preserve the blood supply.

In a few cases I have observed irritation, and in two, even sloughing out of the silk without actual infection. Chromic catgut was therefore used in three cases, but Steinach and his surgeon strongly advise the use of silk, as it excludes the possibility of a re-opening of the vas. I am personally now using nothing else, but insist on double sterilization of the silk.

The place of the incision varied. I have either exposed the vas near the root of the penis or incised the scrotum and ligated near the epididymis. A somewhat quicker result can perhaps be looked for after the latter procedure. I have nowhere ligated between epididymis and testis.

†N. York M. J. [etc.]), 1922, **114**, 687; Ibid., 1922, **116**, 203; Am. **Med.**, 1922, **28**, 435.

According to Steinach's theory, ligation of the vas (not vasectomy alone) causes through back-pressure and later inactivity an atrophy of the generative portion of the testis, with subsequent proliferation of the so-called puberty-gland, consisting mainly of the interstitial (Leydig) cells. The increased formation of gonadal hormone re-activates the entire endocrine system of the patient, causing clinical results, varying from nothing more than an "endocrine tonic" to an almost actual "re-juvenation."

As an indication for the operation,—speaking generally and from an endocrine point of view—I have taken a hypofunction of the gonads, or better, an inferiority in the gonadal activity. I have assumed that "senility" is due to a naturally occurring, i. e., an acquired hypo-gonadism (primarily or secondarily) with an accompanying dysfunction of the rest of the incretory organs. If this state of affairs exists at a relatively early stage of life, I speak of "premature senility." Here, congenital inferiority of the gonads or the whole endocrine system plays perhaps a rôle. Such endocrine constitutional inferiority, or weakness of the gonads I also assumed in certain cases of sexual impotence (those of gonadal origin). Here the other endocrine organs are not affected in the same sense, and no symptoms of general senility are apparent. Those cases have also been described as "partial senility" and "partial premature senility," by Schmidt.

The principal contra-indications were: Advanced senility with atrophic testes, and a seriously impaired cardio-vascular apparatus. I have also refused the operation where it seemed that other therapeutic procedures, for instance, rest, should first be tried for symptoms of senility and where evidence of organic defects, like tabes, existed, to explain sexual impotence.

The important questions arise: Where can we expect fairly good results, where excellent ones, in what cases none at all, and can harm be done in ligating a man's vas, causing him to form a new puberty gland? The last question I am inclined to answer with "No." We have no proof whatever of any injurious effects, all the evidence pointing to the harmlessness of the procedure. Even where additional gonadal hormone is not required, we can trust in the balancing power of the endocrine apparatus as a whole. To the other questions I cannot give a definite answer,

but would like to suggest a way of examination and classification which may in the future, and based on larger clinical material, enable us to understand more clearly the endocrinological consequences of the vasoligation, and thus differentiate favorable from unfavorable cases. I have therefore attempted to classify all cases according to their endocrinological "constitution," taking into consideration their life history, the character of their complaints, and their physical make-up. I have designated them as "thyroidal," "gonadal," etc., and where two glands seemed to be prominent in the patient's constitution, I described them as "thyro-gonadal," "pituito-adrenal," etc., putting the one most likely primarily delinquent in the first place. I have not differentiated between "hypo" and "hyper," unless this was glaringly justified.

I have interpreted the patient's symptoms from an endocrine point of view as far as possible, and likewise the changes that appeared after the operation. Then, taking the patient's constitution into consideration, I have sought to answer the question which constitution offers the best chances and in the sphere of which gland the principal changes might develop. This means clinically: Which are the favorable cases, and what will happen to them after the operation.

In view of the modernity of endocrine studies, a divergence of opinion might naturally arise regarding the classification of the constitution and the interpretation of symptoms. The study of more data is therefore imperative.*

The complaints of the senile cases were of the usual nature, partly mental and partly physical, and need not be described in detail.

The age in the 22 cases reported lay between 36 and 64. They consist of (1) 12 cases of senility including premature and physiological old age (acquired gonadal deficiency); (2) 8 cases of congenital inferiority of gonads (hypogonadism) with sexual impotence; (3) 1 case of dyshormonism (No. 9); (4) 1 case of carcinoma.

Cases 1 to 8 have already been reported elsewhere with clinical details, as previously stated, but at that time I had not touched upon the endocrine aspect.

*It seems fair to state that my endocrine interpretations are based on the plan originated by Dr. Joseph Frankel.

Regarding results, it must be noted that it sometimes takes six months, perhaps even more, for the full quota of clinical effects to develop. Positive improvements within this period give no definite clue as to their final intensity. I have found it practical to classify the results as follows: (1) *Negative,* if no changes at all occurred attributable to the operation, after a period of six months or more; (2) *Subjectively positive and doubtful,* if the patient stated improvements in his subjective sphere only, doubtful regarding endocrine interpretation. These cases have naturally a limited value as scientific evidence; and (3) *Positive,* if clear evidence, for instance objectively, of a beneficial effect was at hand, in some cases naturally only "partial."

ENDOCRINE OBSERVATIONS AND FURTHER STUDY OF EIGHT CASES, PREVIOUSLY REPORTED

Case 1. Clerk—58 Years

Diagnosis: Premature senility with mental depression and varicocele.

Constitution: Adreno-gonadal.

Operation: February 2, 1921, in combination with varicocele (Dr. Reitzfeld). This patient did not know that the Steinach operation was performed.

Last Examination (Dr. Reitzfeld, five months p. o.): Distinct mental and physical improvement; gain in weight of twelve pounds; no change in sexual life; no endocrine study was attempted.

Result: Positive (auto-suggestion excluded).

Case 2. Merchant—57 Years

Diagnosis: Premature senility; chronic arthritis in both knees.

Constitution: Pituito-gonadal.

Operation: November 1, 1921.

Last Examination (seven weeks p. o.): Marked functional improvement in his knees; general condition decidedly improved; sexual power increased; a distinct thyro-pituito-gonadal influence apparently manifest, but the time of observation too short to draw reliable conclusions.

Result: Subjectively positive (Doubtful).

Case 3. College Professor—55 Years

Diagnosis: Premature senility; prostatic hypertrophy with frequent micturition; affection of the internal ear (sclerosis) with increasing deafness.

Constitution: Pituito-gonadal.

Operation: December 28, 1921.

Last Examination (seven month p. o.): Marked improvement in every way; hearing much better as proved by objective methods (Dr. Max Heimann); prostate smaller, urination normal; weight increased by six pounds; blood pressure constantly somewhat lower, within normal limits; sex-life unchanged.

Endocrine interpretation is doubtful; thyroidal and pituitary activity is improved. The effect in the gonadal sphere seems to have influenced the prostate only. For the libido the cortex cerebri is too

important and perhaps only influenced by the gonads when psychic factors are favorable. This was not the case here.

Result: Positive.

CASE 4. MANUFACTURER—48 YEARS

Diagnosis: Premature senility; marked sexual impotence (not improved by transplantation of human (?) testicle or any other treatment).

Constitution: Adreno-gonadal.

Operation: February 15, 1922 (ligature had possibly sloughed out).

Last Examination (four months p. o.): General improvement physically and mentally; gain in weight ten pounds at least; sexual ability decidedly better but not yet normal; nightly emissions occurred first time in several years; increase in libido very doubtful.

Thyro-adreno-gonadal influence is apparent, but only in a moderate degree.

Result: Partially positive.

CASE 5. LABORER—38 YEARS

Diagnosis: Premature senility with sexual impotence; varicocele.

Constitution: Thyro-adrenal.

Operation: February 20, 1922.

Last Examination (March 30, 1922): No definite changes.

Result: Patient could not be reached for re-examination; negative, six weeks p. o. Case not classified.

CASE 6. CONTRACTOR—58 YEARS

Diagnosis: Senility (premature).

Constitution: Adrenal.

Operation: February 28, 1922.

Last Examination (August 18, 1922, 5½ months p. o.): Marked improvement; more ambition and no more mental depression; gain of about six pounds in weight; appearance much better, complexion markedly improved; former frequent urination normal.

Patient says that he perspires more freely than in former years, and also noticed a stronger growth of his beard, as evidenced by necessity of more frequent shaving. His blood pressure (syst.) was around 180; is now 150. Pulse pressure has decreased from 85 to 75. His prostate showed a distinct hypertrophy, especially of the left lobe. It is still large, but both lobes alike, the left one having decreased in size. The skin reaction has changed from faintly red with white borders to a distinct red line of long standing. He feels perfectly able to resume business responsibilities which he had dropped for years. Sex desire and ability has increased little if any.

Here the changes in perspiration, complexion, growth of beard, blood-pressure and skin reaction indicate increased thyroid activity, balancing the (constitutional) adrenal dysfunction, as evidenced by blood pressure and skin reaction (Sergent line).

Result: Strongly positive.

CASE 7. WATCHMAKER—36 YEARS

Diagnosis: Sexual impotence for the last nine years; premature senility.

Constitution: Gonadal.

Operation: March 6, 1922.

Last Examination (August 16, 1922, 5½ months p. o.): Decided mental and physical improvement; patient has returned to work that he had discontinued for many months; feels as well and ambitious as ever; more self-assurance; acne on back disappeared.

The patient volunteered two interesting statements: First, he

had been using a 2½-inch focus magnifying glass for his work which he finds too strong now; is using a 3½-inch focus now; second, has to shave every day compared with every two to three days formerly; he claims that his hair is growing "awfully fast." Sexual impotence is practically cured and he has had sexual intercourse satisfactorily for the first time in the last 9 years. He intends to get married.

Here also the thyroidal stimulation is evident, in addition to the increased gonadal activity in accordance with his constitution.

Result: Strongly positive.

CASE 8. EDITOR—58 YEARS

Diagnosis: Premature senility.

Constitution: Pituitary-adrenal.

Operation: March 15, 1922.

Last Examination (August 18, 1922; 5 months p. o.): All physical and mental complaints have completely disappeared, especially his frequent (pituitary) headaches; enjoys perfect health; skin reaction has changed from red with white borders to distinctly red; (syst.) blood and pulse-pressure have dropped 10 mm. within normal limit; sexual limitations are unchanged.

In accordance with the patient's constitution the balancing of the pituitary and adrenal dysfunction is very evident. This patient is a highly intelligent and critical man. No change in the gonadal sphere is apparent.

Result: Positive (except sexually).

For additional details as to symptoms and other clinical data of the above eight cases, I wish to refer to my previous publication of August 31st, 1922, in "Am. Med."

PRELIMINARY REPORT OF 14 ADDITIONAL CASES

CASE 9. ENGINEER—36 YEARS (REFERRED BY DRS. D. M. KAPLAN AND GREG. STRAGNELL)

Principal Complaints and Symptoms: Patient feels physically and mentally "inferior"; has frequent (pituitary) headaches and digestive disturbances; suffers from premature ejaculation and partial sexual impotence.

Diagnosis: Dyspituitarism with secondary dysgonadism; giantism; varicocele; scoliosis; chronic otitis media with moderate deafness.

Constitution: Pituitary.

Operation: March 17, 1922, in combination with partial resection of the varicocele (the Steinach operation was performed as an attempt to influence the endocrine system); a part of the silk ligature sloughed out without infection.

Last Examination (3½ months p. o.): After "ups and downs" doubtful as to resulting from operation, the patient now states that his headaches have decidedly improved in that they are less frequent and less intense; better digestion; sex desire irregular but more frequent nightly emissions; no opportunity to test his potency; no objective changes in weight, blood pressure, etc.

Result: Doubtful, subjectively positive (although the improvement suggests an influence on his constitutionally inferior pituitary).

CASE 10. DENTIST—39 YEARS. (REFERRED BY DR. STRIKLER OF PHILADELPHIA)

Principal Complaints and Symptoms: Sexual weakness began four years ago; now complete impotence; 25 years ago contracted syphilis that was treated until several Wassermann examinations of blood and one of spinal fluid were negative; knee jerks distinctly exaggerated, otherwise physical examination negative.

Diagnosis: Impotentia sexualis somatica; psoriasis; lues (cured?).
Constitution: Adrenal.
Operation: March 17, 1922.
Report by letter: No change (2½ months p. o.).
Result: So far negative.

Case 11. Agent—56 Years

Principal Complaints and Symptoms: Fifteen years ago one kidney removed on account of stones; frequent attacks of dizziness; poor memory and lack of ambition; slight deafness; glycosuria, disappearing after a few days of strict diet.
Blood Pressure: (Syst.) between 160 and 170; pulse pressure between 60 and 80; weight, 138 pounds; no skin reaction; sex desire and ability gradually waning; prostate enlarged; occasional slight attacks of gout; irritable and depressed.
Diagnosis: Premature senility; beginning arteriosclerosis; diabetes mellitus.
Constitution: Thyro-adrenal.
Operation: March 27, 1922. (Healing of wound delayed.)
Last Examination (4½ months p. o.): In the intervening time there were "ups and downs" in patient's subjective complaints; no improvement in his sugar tolerance and in his sexual limitation apparent; indigestion, probably due to his lack of teeth and inability to masticate properly; less depressed and somewhat more ambition; generally livelier, looks better and hears better as noticed by his relatives; his skin reaction, faintly red; his weight slightly increased (140 pounds); his attacks of dizziness practically ceased since about 4 weeks p. o.; his blood pressure dropped and now changes between 130 and 145, syst.; pulse pressure between 45 and 55.
So far only slight stimulation of thyroidal activity seems to manifest itself, with subsequent effect on the adrenals.
Patient's improved hearing has been confirmed through objective methods by an ear specialist (Dr. Max Heimann).
Result: Partially positive.

Case 12. Naval Officer—53 Years

Diagnosis: Beginning arteriosclerosis; angina pectoris.
Constitution: Adreno-gonadal.
Principal Symptoms and Complaints: Mild but frequent attacks in heart region, radiating into left arm, occasionally quite severe; blood pressure, systolic, 155; diastolic, 110; pulse, 76.
X-ray examination of heart showed moderate enlargement of heart and aorta; weight 161½ pounds; sexual ability decreasing; prostate enlarged.
Operation: April 11, 1922; one month after the operation the subjective condition was about the same, but patient noticed stronger erections; his blood pressure, systolic, 135; diastolic, 90; weight, 163 pounds; otherwise no change.
Case not classified.

Case 13. Importer—43 Years

Diagnosis: Hypo-gonadism; sexual weakness.
Constitution: Gonado-pituitary.
Principal Complaints and Symptoms: Patient feels that through his sexual inferiority (weak desire as well as limited potency) he "is losing something in life"; desires marriage; fears premature senility.
Operation: April 21, 1922 (ligation with chromic catgut).
Although no re-examination has been possible, the patient reported (5 months after operation) that no noticeable changes have occurred

in his condition. He is in excellent health, physically and mentally. I am, however, inclined to classify his case as

Result: So far negative.

CASE 14. DENTIST—53 YEARS

Diagnosis: Premature senility; beginning arteriosclerosis; impotentia sexualis; doubtful syphilitic history.

Constitution: Adrenal-gonadal.

Principal Symptoms and Complaints: Nervous twitchings; insomnia; increasing weakness of sight and hearing; lack of "pep"; shortness of breath on exertion; sexual impotence for the last 10 years; x-ray examination of heart (Dr. Philips) shows a moderate general hypertrophy without insufficiency or dilation; blood pressure, systolic, around 140; pulse pressure, 60; pulse, 76-80; weight, 155½ pounds.

Operation: April 29, 1922 (ligated bilaterally with chromic catgut).

Examination (one month p. o.): Patient claims to have more energy and ambition, but only since a few days; also distinctly better erections, but no intercourse attempted; blood pressure, systolic, 122; pulse pressure, 37; pulse, 64; weight, 159½ pounds (4-pound gain). In a letter of July 31st from out of town, patient reported to be in about the same condition as on the last examination.

So far an influence on the adrenals and in the gonadal sphere is evident. Although objective changes seem to have occurred, the time of observation was too short to call the result so far other than doubtful.

Result: Doubtful.

CASE 15. MERCHANT—63 YEARS

Diagnosis: Beginning senility.

Constitution: Pituito-gonadal.

Principal Symptoms and Complaints: Patient feels that oncoming of age interferes with his ability to work, especially in regard to memory, ambition, power of concentration, etc.; blood pressure, systolic, 138; pulse pressure, 58; prostate enlarged.

Operation: May 3, 1922 (ligation with chromic catgut). (Traumatic non-infectious epididymitis followed, but healed promptly.)

A letter of August 5th (three months p. o.) reads in part: ". . . I am feeling fine since the operation. There has been a general improvement in my health, particularly the prostate trouble. I have gained some flesh. I cannot see that my sex powers have increased to any extent. . . ."

(No endocrine interpretation attempted from written reports.)

Case not classified.

CASE 16. ELECTRICIAN—39 YEARS

Diagnosis: Premature senility; sexual impotence.

Constitution: Thyro-gonadal.

Principal Symptoms and Complaints: Mentally depressed, cannot keep a good position through lack of ambition; premature ejaculation amounting to sexual impotence that depresses him greatly; looks almost senile—about 15 years older than his age; organic mitral heart lesion well compensated; blood pressure, systolic, 142; pulse pressure, 32; weight, 136 pounds.

Operation: May 26, 1922.

Examination: June 5, 1922. Blood pressure, systolic, 115; pulse pressure, 30; weight, 137¾; no change of subjective symptoms.

Since no further report has been received of this patient, his case has not been classified.

CASE 17. CLERK—55 YEARS

Diagnosis: Carcinoma of head of pancreas.

Constitution: Thyro-adrenal.

Principal Complaints and Symptoms: Pain in stomach and loss of weight; obstructive jaundice; blood pressure, systolic, 130; pulse pressure, 45.

Operation: June 1, 1922.

Dr. Heckman performed laparotomy, found cancer inoperable, adherent to vena cava and aorta; metastasis in liver; bilateral Steinach operation near epididymis.

Last Examination, August 1, 1922 (two months p. o.): The patient has had 6 x-ray treatments (Dr. Thos. Scholz); subjective complaints diminished; weight about the same as after the operation; blood pressure, systolic, 108; pulse pressure, 33; strength not decreased; feels "lots of physical and mental energy"; the intensity of the icterus changed, now about the same as shortly after the operation; patient left town.

A change in the size of the palpable tumor was not evident; however, his constitutional thyro-adrenal sphere shows certain signs of being influenced. The cancer-chachexia has certainly not increased in the two months after the operation.

At the end of September (4 months after the operation), according to his son's report, patient still holding his own; had been traveling a good deal; digestive disturbances distinctly improved; lost no more weight and felt quite satisfied.

Result: So far doubtful, perhaps partially positive.

CASE 18. PHYSICIAN—64 YEARS

Diagnosis: Beginning senility; arteriosclerosis.

Constitution: Adreno-gonadal.

Principal Symptoms and Complaints: Decreasing mental faculties; poorer memory; very irritable; increasing sexual weakness; blood pressure, systolic, 195; pulse pressure, 85; weight, 161; prostate slightly enlarged.

Operation: June 27, 1922; in a letter dated August 5th (about 5 weeks p. o.), the doctor writes: ". . . I began to improve every day after I left the hospital. Have gained in flesh and now weigh 172 in my light weight clothes. I feel that my manhood is very much improved and I took my blood pressure this morning, systolic, 175, and diastolic, 120. . . ."

(His pulse pressure was 55, as compared to 85.) "Everybody tells me I am looking better than when I left for New York."

Considering that this patient is a physician himself, I am inclined to call the

Result: So far, partially positive.

CASE 19. PHARMACIST—38 YEARS

Diagnosis: Impotentia sexualis somatica (hypo-gonadism).

Constitution: Gonado-(hypo)-adrenal.

Principal Symptoms and Complaints: Premature ejaculation with erections rare and considerably weaker than in former years; all treatments including organotherapy unsuccessful; happiness of his married life greatly endangered; mental depression; blood pressure, 140; pulse pressure, 60; weight, 159 pounds.

Operation: August 4, 1922.

Not classified.

CASE 20. DYER—39 YEARS

Diagnosis: Hypogonadism; impotentia sexualis.

Constitution: Thyro-gonadal (hypo-gonadal).

Principal Symptoms and Complaints: Decreasing sexual ability with frequent mental depression; all treatments unsuccessful; right testis slightly atrophic through accident in childhood.

Operation: August 7, 1922.

Examination, August 19, 1922: Patient had a pollution two nights ago, first in many months; is sure that erections are stronger; blood pressure, systolic, 110, compared to 122 before operation; pulse pressure, 40, compared to 42; no other change.

Here ten days after the operation, a greater activity in his constitutionally inferior gonadal sphere seems already to manifest itself.

Last Examination, September 16 (5 weeks after operation): Distinct improvement; unusual sense of well-being; "rheumatic" pains in knees disappeared; pulse, blood pressure, and skin reaction normal as before operation; can read without glasses much easier than before; sexually, a marked improvement; erections are a good deal better; ejaculation still somewhat premature, but more pleasurable.

The improvement of gonadal activity is still more apparent and since the patient does not belong to the class of psychopaths I would already call the

Result: Positive.

CASE 21. PATROLMAN—45 YEARS

Diagnosis: Hypo-gonadism; sexual impotence.

Constitution: Gonad-(hypo)-thyroidal.

Principal Symptoms and Complaints: Decline of sexual ability for the past seven years; all treatments unsuccessful; testes somewhat undersized; skin reaction, white line.

Operation: August 8, 1922.

Last Examination, September 26 (6 weeks p. o.): Patient feels generally unusually well, but has so far not noticed any increase in sexual powers, except for a few days immediately after the operation; nervous temperament still the same; temporary decrease of blood pressure, then return to normal; skin reaction changed into a red line with slightly white borders; gained about 6 pounds in weight.

Increased thyroidal activity seems very probable, but in the gonadal sphere no changes have occurred, therefore,

Result: So far negative.

CASE 22. MUSIC TEACHER—54 YEARS

Diagnosis: Beginning senility.

Constitution: Thyroidal.

Principal Symptoms and Complaints: Decline in mental and physical capacities for past 4 years; endurance, concentration and memory weakened; position endangered; was asked to resign on account of advancing age; frequent urination; prostate enlarged; blood pressure, systolic, 155; pulse pressure, 50; weight, 155½ pounds; sexual ability decreasing.

Operation: August 8, 1922.

In a letter of September 1 (3 weeks after the operation) patient reports very hopefully, emphasizing especially a distinct improvement in urination, the urine flowing "with a much freer and fuller flow than it has for years"; a distinct increase in frequency and strength of erections also noted. No re-examination has so far been possible. I have, therefore, not classified this case at all.

CONCLUSIONS AND SUMMARY

Although being far from having arrived at definite conclusions, I believe that certain observations are sufficiently suggestive to form at least a plausible working basis. Of the 22 cases,

6 were not classified, since no report was received about their condition. The results, therefore, can only be judged in 16 cases. Of these, I consider 9 positive (more or less strongly); 4 doubtful or subjectively positive; 3 negative. The doubtful and negative cases may have to be judged differently after longer observation.

Regarding the endocrine manifestations, I would like to summarize my observations as follows, giving a theory more than scientific facts.

The most frequent and most prominent clinical manifestations as the result of the new activity of the puberty glands seem to be due to increased thyroid activity.

Outside of the thyroid, the re-activated puberty gland seems to influence essentially those glands that are most prominent or delinquent in the patient's constitution.

Distinct changes in the gonadal sphere appeared mostly in patients with a gonadal or partly gonadal constitution. Therefore, the claim of certain German investigators that the increase of sexual activity was *regularly* observed could not be fully substantiated.

The following, however, must be considered as well established scientific facts, also deduced from the above observations.

The Steinach operation increases the activity of the puberty gland. This re-activation has an influence on the endocrine system in the sense of stimulation, regeneration, and restoration of equilibrium. No injurious effects have been observed.

Regarding prognosis, I can at present express only a very vague opinion that gonadal or partly gonadal constitution seem to be most promising. I believe that a further close observation of the treated cases from an endocrine point of view will greatly enhance our knowledge of the inter-relationship of the different glands, especially the inter-relationship of the gonads with the rest of the endocrines.

AN ANALYSIS OF ONE THOUSAND TESTICULAR SUBSTANCE IMPLANTATIONS

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In presenting this phase of the study of internal secretions, one cannot be unmindful of the publicity which has been given the so-called interstitial gland during the past three years, and of the bad impression this has made upon the medical world.

The rather doubting, skeptical—even intolerant—attitude of the medical profession toward a subject which has been so largely flouted before the public by newspapers, eager for sensational discoveries, particularly along sex lines, can well be condoned.

In the past, physicians have had their fill of the "lost manhood" charlatans. And when word came from abroad in 1918 that youth could be renewed and many of the potentialities restored by the engrafting of interstitial glands of the monkey, the medical profession for the most part ridiculed it, feeling that it was similar in purpose and intent to the widely heralded tuberculosis cure with turtle serum coming from Germany in 1913.

The public, however, clamored for more news about this wonderful and all-absorbing topic, with its mystery and sex-appeal. It became a very interesting subject of conversation among men as well as women in all walks of life.

Soon after Voronoff brought forth this monkey gland announcement, it was emphasized that Lydston of Chicago had been doing similar work with human material since 1913, and that the medical department of the California State Prison had, following his example, been transplanting testicles from recently executed convicts to senile and devitalized men for some time.

Brown-Séquard, in experimenting on himself in 1889, found that by injecting an extract derived from the testicles of dogs, definite dynamic effects were produced. He regained much of his former strength, fatigued less easily, and was able to do work greatly in excess of what he had been capable of before. His

mental faculties were increased, and intellectual efforts became easier. He noticed that he was greatly relieved of constipation, and believed that the testicular extract had an influence, particularly on the spinal cord.

Because of the activities of quacks and charlatans in the time of Brown-Séquard, the complete investigations of this extract were not fully carried out as they should have been. With his experiments, however, an interest in the study of internal secretions was aroused. Indeed, this work marks the "birthday of endocrinology," as such.

This paper deals with one thousand injections of animal testicular substance into 656 human beings. The greater number received only one injection, while to some were administered as many as seven. Among the patients treated were ninety-six unconfined people, including thirteen physicians and seven females. The remaining five hundred and fifty were inmates of the state's prison. This does not include the twenty cases in which human testicles were transplanted from executed convicts to others. But it does include about ninety cases in which a piece of ram's testicle the size of a dollar was implanted by operation into the scrotum or abdominal wall.

It was found that these heterogenous grafts were gradually absorbed. In order to obviate operation in which the rectus fascia of the abdomen was exposed and an implant inserted, a syringe method of implantation was devised. Immediately after the death of the animal, the scrotum with the testicles enclosed was tied off and cut away. This was then taken to the operating room, where the external hair or wool was clipped off and the skin painted with iodine. It was then incised longitudinally, and the cut edges retracted and held away with haemostats. Using other scissors and sterile clamps, the next of the many coats of the dartos fascia were likewise opened, until the tunica vaginalis was reached. The tunica was in like manner incised and retracted, revealing the perfectly aseptic testicle enclosed. This was seized with a tenaculum and withdrawn entirely free of contamination. The epididymis and surrounding tissues were then cut away.

The testicular substance was cut into strips with a knife or cork-borer, in sizes suitable for the filling of the pressure syringe. This instrument is similar to the one devised by Beck for paraffin

injection. A dental syringe with a No. 16 needle, 3½ inches long, has been found to be satisfactory.

By this means the semi-solid testicular substance was injected by force underneath the skin of the abdomen. With this method there were comparatively few sloughs, and the patient was not subjected to a week's hospital inconvenience.

The testicles of goats, rams, boars and deer have been used. So far as can be determined there is very little difference in the effects produced by testicular material obtained from various animals.

The first of these cases was treated in January, 1920, and the last in February, 1922.

In order to see if there were any therapeutic value in this procedure, and if possible to determine what cases, if any, might be benefited, anyone who applied was given treatment. The matter was fully explained to the patient, and he was allowed to use his own judgment as to whether he cared to submit or not.

It was probably fortunate that this work could be carried out in a prison, for in such a place all men are treated alike, and live under the same conditions of food, work, and general surroundings. A good opportunity was given for observing the results, because the patients could be under daily observation, and the "follow-up" conditions were ideal.

As soon as a new prisoner is received at San Quentin, he is given a thorough physical examination, so that his status at entrance is well known. Any changes taking place in the condition of the prisoner can be easily checked up.

In starting this analysis, it might be said that eleven of the patients are now dead. One is thought to have committed suicide, one died of uraemia, three of pneumonia, and six succumbed to tuberculosis.

From a compilation and study of data from these 1000 treatments, it is believed that testicular substances do have a decided effect on conditions of general asthenia. This term is applied to patients who are underweight, lack energy, sleep poorly, have scant appetite, and, to use their own expression, are "all run down." With them nothing definitely pathological can be found. Usually within the first week after the treatment they gain in weight, have increased appetite, enjoy their work, and evince a general buoyancy. Of the 326 patients so diagnosed,

305 have shown by their actions, by their weight, and by their own written reports that they have been markedly benefited. None who have been so afflicted and have received the treatment became worse, but a few did not improve.

In the early experimentation, it was thought that the goal to be reached, and the proof of the treatment, was sexual stimulation. Usually with a relief from an asthenic condition, the sexual manifestations appear as the patient regains normality. If his general condition is below par, his sexual desires may be somewhat lethargic.

Of the total number of patients, 81 reported increased sexual stimulation. This was evidenced to them by frequent erotic dreams with emissions, and frequent erections without undue sexual cause.

It can hardly be said that this treatment cures impotency, although some who have not had sexual manifestations for years have a renewal of this function. On the other hand, three men who claim that they were normal sexually before the testicular substance injections report that their potentialities in this respect have almost entirely faded away.

The difficult problem in this investigation, as in any other regarding health, is to know just how much reliance can be placed in the patient's own statements and observations.

Prisoners as a rule are antagonistic; that is, they are against the officials who have anything to do with their incarceration. The state put them in prison—they are against the state. The officials represent the state—hence they are against the officials. This is mentioned merely to show that anything done by officers of the medical department, or any other department in the prison, would be harshly criticised by them if no benefit were derived from it.

With the gland treatment, however, most of those who took it give a fair and truthful report as nearly as can be determined.

After a few of the men had undergone the injection and found that there was little pain to it, and that they were benefited, they told the other inmates and as a result there were many applications. Instead of being against the treatment, they were for it, even overcoming their natural tendency to oppose.

One of the skin diseases most resistent to treatment is acne. This affection frequently comes at that transition period, when

the youth is entering manhood. Usually after several years it disappears. Among the 656 patients treated with testicular substance, 66 had this disease.

It can be said that acne is markedly influenced by this treatment. One does not have to rely upon the statement of the patient in this regard, for the improvement in the face can be seen. Photographs have been taken before and after the implantation. The acne does not dry up as if by magic, but the number of pimples decrease and very few comedones appear when they are once removed.

Whether testicular substance contains some inherent power like adrenalin to influence asthma, or whether by means of a hormone sent into the blood stream, acting upon the adrenal glands, adrenalin is elaborated, and thus alleviates asthma, is not known. But of the 21 patients of this series who suffered from asthma, 18 secured relief or had the severity of their attacks greatly decreased.

One man, aged 23, who had had asthma all his life, has been given four injections at intervals of three or four months. His arms were badly pocked where he had taken adrenalin by hypodermic. At the present time he rarely has an asthmatic attack. Others give somewhat similar histories. Three of the asthmatic patients have had no relief.

In asthma, as in all other conditions treated, it has been found that sometimes one injection of a dram of testicular substance does not have an appreciable effect. A subsequent injection may, however, prove of benefit. This may be due to the presence or absence of some body in the testicles of one animal that is not in another. This of course is only conjecture.

In some patients the substance injected will remain under the skin and be plainly felt as a shot-like body for several months, while in others it disappears within a few weeks.

The possible advantage of using the whole testicular substance, instead of the extract as Brown-Séquard did, is that it is absorbed so slowly that in this process of absorption the hormone is gradually given off, producing a continuous effect. The extract may be absorbed within a few hours.

There were four cases of diabetes. Three of these claimed improvement, in that they gained in weight and improved in general condition. One man, aged 67, had had diabetes for nine

years, his urine was full of sugar, and there was some gangrene of his toes. He was given two treatments of testicular substance in February and May of 1921. In October he was transferred to Folsom prison, where Dr. Clattenburg, the resident physician, reported that, although this man partook very freely of Christmas candy and pastry, he was unable to find any sugar in the urine after repeated tests.

Three subjects having locomotor ataxia claim that the pains were lessened and that they felt better. Of course, the disease was in no way arrested. It seems that in some way this therapeutic agent has some influence in pain.

Fifty-eight of the patients treated complained of rheumatism. By this term is meant those pains in the back, shoulder and legs for which no definite cause can be found. Forty-nine claimed that their pains have stopped, while four found no difference, and five reported their condition slightly worse. In this connection it might be said that several affirm that cramps in their legs have disappeared.

Among the patients treated, thirty-four were senile. Twenty-seven of them showed improvement in that they were more energetic, ate better, and showed more activity mentally and physically. The observations made on these old men were in many respects similar to those which Brown-Séquard made on himself.

The results in tuberculosis have not been particularly encouraging, for, as previously stated, six of the seventeen patients so afflicted died. Of the others, 10 are benefited by increase in weight and appetite. Those who died were in advanced stages of the disease. One woman with pulmonary lesions gained fifteen pounds, and in spite of afterward contracting influenza, subsequently gained two pounds additional.

Fifty-six patients were suffering from neurasthenia. Some of them were the "hospital pests," never benefited by anything. Of this number, however, thirty-three cases showed decided improvement. They gained in weight, felt fine, and apparently forgot many of their fancied ailments.

It has often been asked what part psychology plays in this treatment. To be sure, that is to be thought of. But it can hardly be said that psychology will influence asthma, or benefit acne, or, without other stimulation, spur up the sexually dor-

mant. The marked improvement in the general asthenic cannot well be placed at the door of psychology.

All of the thirteen physicians who took the treatment, with the exception of one, reported good results. It is extremely doubtful whether auto-suggestion entered into their case.

In their reports, many of the patients claimed that they have been relieved of constipation. No data has been kept on this phase of the subject. Nor have any data been compiled, in these experiments, on blood pressure.

Forty-one of those treated complained of poor vision which necessitated glasses. Thirty-two report that their vision was greatly strengthened after the implantation. One man, an official of the prison, declares that before his treatment he had difficulty in distinguishing the torpedo boats which ply up and down the bay. Following two injections, he affirms that he is not only able to distinguish the boats, but he can read the numbers on the bow. In addition, this man has gained forty pounds in weight. He is an accountant, and credence should be given his statement.

An endeavor was made to interest occulists in this matter of eye improvement. The work was taken up but was not finished.

There have been found no ill effects resulting from the testicular substance implantations, other than an occasional slough of the material. In those cases which do slough, the site of injections swells, becomes reddened and slightly painful. An incision brings out necrotic material and leucocytes. After a few days this heals over with no great inconvenience.

Four subjects have had edema of the scrotum within a few days after the injection. This soon subsided. There are no bad constitutional effects, such as fever, chills, pains or headache. The patient goes about his work as usual, although he might feel some soreness, and occasionally an itching sensation near the needle wound.

In conclusion it might be said that investigation of this subject is being kept up in the endeavor to seek the truth. Many obstacles are placed in the way and the bad impression which is engendered through publicity and the unwarranted claims of medical buccaneers on this poorly charted sea of research must be overcome.

SUMMARY

The results of 1000 implantations of testicular substance in 656 human subjects, including 7 females, are reported. Striking objective improvement was seen in numerous cases of general asthenia, acne vulgaris, asthma and senility. Subjective or objective improvement was seen in various cases of rheumatism, neurasthenia, poor vision and a few other conditions. The results as a whole are tabulated. In general testicular substance seems often to have a beneficial effect in relieving pain of obscure origin and promotion of bodily well being. The operation is practically painless and harmless.

ANALYSIS OF CASES

	Total Cases	Benefited	Not Benefited
General asthenia	336	305	31
Rheumatism	58	49	9
Acne vulgaris	66	54	12
Neurasthenia	56	33	23
Poor vision	41	32	9
Asthma	21	18	3
Tuberculosis	17	10	7
Senility	34	27	7
Sex lassitude	95	81	14
Impotence	19	12	7
Psychopathic inferiority	8	..	8
Epilepsy	5	3	2
Dementia praecox	8	1	7
Paranoia	3	2	1
Diabetes	4	3	1
Locomotor-ataxia	3	3	..
Drug addicts	32	..	..
Dead	11	..	..
Unclassified	28	..	..
No report	30	..	..

CONCERNING THE PATHOGENESIS OF THYROTOXICOSIS. PART II

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THE DYSTHYROIDISM OR DYSFUNCTIONAL THEORY

In the preceding section of this article, published in the September issue, the various theories of the pathogenesis of exophthalmic goiter were summarized and critically considered. In particular, evidence was offered that the common conception of Graves' disease as due merely to "hyperthyroidism" is untenable. In the succeeding paragraphs evidence will be adduced that the disease represents not "hyperthyroidism" but dysthyroidism.

If we accept that the neurogenous and hyperthyroidism theories are untenable, it must still be borne in mind that the source of the clinical phenomena of Graves' disease lies unquestionably in the thyroid gland itself, no matter whether the ultimate, morbid stimulus originates without or within the gland or both. Objectively considered, there remains then but one other possible explanation for the symptoms and signs of this clinical disorder, namely, that they are the result of an *abnormal* metabolism of the thyroid gland, *i. e.*, a *dysfunctional* condition. This is at direct variance with the conception of primary hyperplasia, an accelerated normal metabolism and a hyperfunctional condition of the gland. The dysthyroidism theory accepts a "qualitatively altered secretion" as responsible for the general symptoms and signs of the disease. Among those supporting this view are some of the closest students of Graves' disease: Oswald, Minnich, Murray, von Leube, Howard, West, Dock, Marine and Lenhart, and McCarrison. The dysthyroidism theory is based upon etiologic, pathologic, metabolic and clinical data which now follow in detail.

ETIOLOGIC DATA SUPPORTING THE DYSTHYROIDISM THEORY

As is well known, thyrotoxicosis is liable to occur in families showing a tendency to goiter and hypothyroidism. In indi-

viduals of the same family, certain members may exhibit thyrotoxicosis, others hypothyroidism. A mother with myxedema, reported by Maude, bore two children, both of whom later developed Graves' disease. Murray and other writers cite similar instances. The familial occurrence would bespeak a common origin and etiologic relationship of the two clinical conditions.

The etiologic relationship of goiter to Graves' disease is important. According to the brilliant researches of Marine and Lenhart, and also Gaylord, on thyroid hyperplasia, adenomatous goiters may be properly regarded as caused by toxic or other agents inducing primary cellular injury or exhaustion followed by secondary hyperplasia. (See succeeding section.) That thyrotoxicosis is likely to develop in such instances has been shown by Wilson, Plummer and Boothby of the Mayo Clinic. Thus, of 1,402 thyrotoxic cases recently reported by Boothby (15), 366 developed thyroadenomata after periods averaging 16 years after appearance of the goiter. If we agree with Marine and Lenhart's well substantiated arguments on the compensatory nature of *all* thyroid hyperplasias, then we must accept that all toxic thyroadenomata develop in glands showing previously cellular proliferation due to toxic or other injury, therefore in a potential hypofunctional condition. This consideration is a strong argument against the conception of a primary idiopathic hyperfunction and for the dysthyroidism hypothesis in the genesis of Graves' disease.

The infectious origin of Graves' disease seems clear in a number of cases. The symptoms are known to appear as a sequela to acute thyroiditis following trauma or by extension from neighboring foci; also after typhoid fever, tuberculosis and other bacterial infections. They sometimes can be traced to remote focal infections. According to the experience of McCarrison (44), Lane (45), Bate (46), Ebstein (47), and others, including the present writer, chronic intestinal toxemia is probably an etiologic factor in another group of cases. It may be noted that these same etiologic factors are frequently demonstrable in simple and endemic goiter (McCarrison). It may, then, be reasonably argued that the subsequent pathologic changes with clinical symptoms of thyrotoxic or hypothyroid type would be explicable on a common basis.

PATHOLOGICAL EVIDENCE IN FAVOR OF THE DYSTHYROIDISM THEORY

The Nature of Thyroid Hyperplasia. It is believed that the "hyperthyroidism theory" has long obscured a clear conception of thyroid pathology and clinical deductions made therefrom. As long as we continue to regard hypertrophy and hyperplasia of the thyroid as good and sufficient evidence of hypothetical "hyperfunction," it remains impossible to correlate and interpret the known facts logically. If, however, the evidence already presented is deemed sufficient to demonstrate the inadequacy of this long accepted view, we are in a position to make unbiased deductions from the data in our possession.

The general nature of hypertrophy and hyperplasia may first be considered. These processes occur: (1) under physiological circumstances in a normal organ when increased function is called for (examples,—increase in size of muscles in athletes, uterine hypertrophy in pregnancy, cardiac hypertrophy in mountaineers, hyperplasia in bone marrow after hemorrhage, etc.); (2) under pathological conditions when through injury to an organ by infection or trauma its function becomes impaired (examples,—hypertrophy of lymph glands, cardiac hypertrophy due to muscular or valvular lesions); (3) as pure growth anomalies (myomata, adenomata, carcinomata, teratomata, etc.), never accompanied by true hyperfunction.

The thyroid gland is one of the most important endocrine organs which control general cellular nutrition and growth. In higher organisms it is the seat of some of the most active metabolism. It is peculiarly reactive to extrinsic stimuli,—nervous, chemical and toxic. Its chief function is the synthesis of thyroxin, the thyroid hormone, a complex organic compound containing about 66 per cent iodine. The careful experimental and clinical work of Kendall and Plummer has made it probable that there is an exact quantum of thyroxin necessary for the maintenance of the normal nutrition of the tissues and organs at any given time. Growth puts an added strain on thyroxin production, since the chief function of the thyroid is anabolic (Janney). All evidence goes to show that the thyroid is under very delicate sympathetic nervous control, in turn influenced by central and very probably by hormonic stimuli—adrenalin—(Cannon, Lenhart and Bowmann). Anatomically and physiologically, the thyroid activity is also stimulated by increased iodine content

of the blood, for which element, because of this gland's peculiar necessity for iodine, it exerts a selective affinity.

To meet these varying requirements rapid physiologic and structural changes are obviously necessary. Among such, normal colloid formation may perhaps be included; this is possibly a means of storage of materials needed in thyroid metabolism. Hypertrophy and hyperplasia occupy a prominent place in such necessary changes. Thus the gland, due to additional requirements of the growing embryo, shows a normal increase in size during pregnancy. Conversely, during inanition it has been experimentally shown to decrease in size as well as to increase in size on meat ingestion (Bensley's opossum experiment). *It is very likely on account of the above causes that hyperplasia is frequently required in the case of the thyroid during the normal course of existence, even when no thyroid disease is present* [White *et al.* (48)].

Marine and Lenhart (49), to whom we are indebted for important studies in this regard, may be quoted as follows:

"In man the greater proportion of thyroids showing histological changes toward goiter formation are not associated with detectable clinical manifestations. Most of these milder degrees of thyroid changes spontaneously right themselves when the underlying or accompanying disease disappears, as, for example, the hyperplasia associated with influenza, or typhoid, or pregnancy, etc., rarely comes to clinical notice. Thus it is that all autopsy series show such a great proportion of thyroid changes without detectable clinical manifestations."

From these considerations, it is evident that hyperplasia in thyroid conditions develops on account of the same causes as in all other organs and tissues and is due to: (1) increased physiological requirements (examples,—goiter of puberty, pregnancy, etc.); (2) decreased function because of trauma, infection and other pathological processes either in the thyroid or in the organism in general (examples,—acute thyroiditis with acinar hyperplasia, thyroid enlargement in acute and chronic infectious diseases, endemic goiter, hyperplasia after thyroidectomy): decreased function due to under-nutrition, including iodine starvation (examples,—goiters in poorly fed puppies, lambs and children).

The Relation of Iodine to Thyroid Structure has been thoroughly studied by Marine and Lenhart, who state:

"Withholding iodin increases the extent of the hyperplasia following partial removal (Marine), and also causes hyperplasia without partial removal (Baumann).

"The administration of iodin causes active hyperplasia of all

animals to revert to the colloid state; prevents the occurrence of active hyperplasia following partial removal of glands which otherwise would undergo hyperplasia.

"The administration of iodin prevents hyperplasia of the thyroids of puppies from bitches in which three-fourths of the gland has been removed.

"Normal thyroids of all the animals examined have the highest and marked hyperplasias, the lowest iodin contents.

"The administration of iodin-containing compounds to the animal in any form and by any method is rapidly followed by its storage in the thyroid in quantities that bear no relation to the iodin content of the other tissues.

"The rapidity of accumulation and the amount of iodin thus taken up by the thyroid depend on its size and the degree of active hyperplasia.

"The physiological activity, as determined by the nitrogen excretion (Roos), by the loss of body weight (Marine and Lenhart), and by the acetonitrile reaction (Hunt, Hunt and Seidell), depends principally on the amount of iodin in organic combination.

"It has been shown (Marine and Williams, Marine and Lenhart) that in dog, sheep, pig, ox and human thyroids there is a quite constant minimum percentage of iodin necessary for the maintenance of normal gland structure.

"While practically nothing is known of the causes leading to the iodin deficiency in the animal, the above facts, beyond doubt, show that the increased growth and divisional activity of the thyroid cells are intimately associated with a decrease in iodin, and that the increased iodin content is similarly associated with a decreased growth and divisional activity of the thyroid cells. On this basis one would expect to find thyroid changes resulting from any cause which diminished the intake or assimilation of, or increased the body demands for iodin, and that, therefore, all thyroid changes would be compensatory in nature and secondary to more fundamental causes, perhaps nutritional in nature."

The Histo-pathology of Thyrotoxicosis and its Relation to the Iodine Content follow the same laws as they do in morbid processes in general and in other thyroid conditions, normal and abnormal. This assertion is based upon the following observations:

1. The histological changes of the thyroid gland in thyrotoxicosis are fundamentally the same as those occurring in other goiters. The differences are chiefly those of degree. The rapidity and succession of periods of hyperplasia and involution also play their part; also the age of the affected individual and the goiter. The hyperplasia of exophthalmic goiter varies with pregnancy or puberty, precisely as do simple goiters. Colloid goiters in thyrotoxic patients are not infrequent.

2. The iodine content of the gland in thyrotoxicosis varies inversely with the degree of hyperplasia and in general is modified by the same influences as in other thyroid conditions. The hyperplasia in thyrotoxic goiters can be reduced by administer-

ing iodine just as is possible in the case of simple goiters. The thyrotoxic goiter is poor in iodine as is simple goiter. Degenerations, atrophy and sclerosis may follow the hyperplastic stage in thyrotoxicosis as in thyroid adenoma with development of myxedema or cretinism in either case (Marine and Lenhart, McCarrison).

3. There is a lack of parallelism between the degree of hyperplasia and the toxic clinical symptoms which would argue for a differing etiology of each and against a direct cause and effect relationship (see also histologic discussion under "hyperthyroidism theory").

The hyperplasia of thyrotoxicosis is best explained, just as in other thyroid hypertrophies, as an attempt at compensatory regeneration to make up for cellular exhaustion and injury due to toxic or other cause. We have thus an acceptable explanation for the thyroid hyperplasia of Graves' disease arising from local or focal infections, intestinal toxemia and bacterial infections,—hyperplasias not susceptible of reasonable explanation by the hyperthyroid theory. In order that the supply of thyroxin under these circumstances be maintained at the normal level, increase in the secretory tissue is necessary in order to compensate for exhaustion of the acinar cells through toxemia.

In thyrotoxic cases arising after nervous shock or exhaustion, the hyperplasia is again explicable on the same general basis. Owing to exaggerated or deficient neuro-trophic stimuli in such cases, an abnormal cellular metabolism is set up with ensuing decrease in the normal quotum of normally functionating parenchyma, which condition elicits the stimulus to rapid hyperplasia.

The pathological processes, then, are essentially the same in all thyroid diseases, aside from the malignant.

They represent themselves by three stages: (1) the hyperplastic; (2) the involuntary, recovery or colloid; (3) the exhaustion or premature atrophy or myxedematous stage (Marine and Lenhart, McCarrison). In exophthalmic goiter, the hyperplastic stage predominates and the morbid process is usually arrested at the first or, more rarely, at the second, or third. Not only may the lesions of thyrotoxic goiter be reasonably explained upon this basis, but also those of endemic goiter and hypothyroidism. In ordinary colloid goiters, the process ceases with the second stage,

whilst in hypothyroidism the atrophic processes predominate, not without, however, frequent secondary development of hyperplasia and colloid formation (goiters of cretins).

This pathological consideration would be incomplete without reference to the work of Wilson (12) and Plummer (13) on the pathological classification of surgical goiter. As is also clearly shown by Boothby's (15) recent presentation of these data, goiters of thyrotoxic patients may be classified into two main groups: (1) toxic adenomata; (2) exophthalmic goiter. The former group is distinguished by the development of discrete adenomatous nodules which only after an average period of 16 years are followed by toxic symptoms. The second type is distinguished by a diffuse parenchymatous hypertrophy followed within a few years, at most, by more severe clinical symptoms, including exophthalmos, thrills, and bruit. Great credit is due these Mayo Clinic workers for the thoroughness with which this differentiation has been worked out in a large number of cases. C. P. Howard (7) has, however, pointed out that a similar classification of thyrotoxic cases had already been present by Buschan (50) in his monograph published in 1894. Plummer, who has long adhered firmly to the hyperthyroidism theory, formerly ascribed both classes of these cases to hyperthyroidism, on the basis of the presence of hyperplasia. In his most recent article (14) he regarded, however, the toxic adenomata as due to "pure hyperthyroidism," but entertains the possibility of an altered thyroxin molecule in the exophthalmic goiter group.

The importance of this grouping from the pathological and clinical standpoint is undoubted. The acceptance, however, of a differing pathogenesis seems scarcely justified by the facts known at present. According to the broad conception of thyroid pathology established by Marine and Lenhart, as well as McCarrison, it is likely that the differing pathological and clinical manifestations are largely merely those of degree, inasmuch as hyperplasia and essentially the same clinical manifestations are present in both classes of cases. The thyroid, in the case of the toxic adenoma, may, through the slow influence of hereditary thyroid deficiency, under-nutrition, or chronic toxemia develop discrete hyperplastic nodules which may suffice to afford a complete compensation as to function (non-toxic thyroadenoma). Only after a prolonged continuance of the exciting factors, a

metabolic disturbance ensues with development of toxic symptoms of a mild type leading but rarely to the severer manifestations of Graves' disease (toxic thyroadenoma). On the other hand in the typical cases of exophthalmic goiter (Group II) the pathological excitant is stronger and the thyroid reaction is more universal (diffuse hyperplasia), but less effectual, since in a much shorter period thereafter and sometimes concurrently, the severe toxic symptoms (exophthalmic, bruit, thrills, greatly increased basal metabolism, etc.) set in. On a similar basis may be explained those peculiar cases of thyrotoxicosis which ensue within a few days after fright or other great emotional shock where the disturbance of metabolism begins before the compensatory hyperplasia has time to become manifest.

The chief difficulty in interpreting the pathological lesions of thyrotoxicosis has, it seems, lain in an over-zealousness to find pathological confirmation of the hyperfunctional hypothesis together with insufficient appreciation of the very considerable variety of factors involved. The frequency of hyperplasia, the low iodine content, and the tendency to late fibrosis in the thyrotoxic goiter would demand evidence of deficient thyroid function in the clinical and metabolic phenomena of the disease. That such evidence may be actually present will now be emphasized.

CLINICAL AND METABOLIC EVIDENCE FAVORING THE DYSTHYROIDISM THEORY

Toxic and Trophic Symptoms. Certain symptoms of thyrotoxicosis are so striking and demand so much attention through their annoying nature that they have always occupied the foreground of attention. The mental changes, the exophthalmos, the tachycardia and tremor may be mentioned. They represent toxic symptoms characteristic of the disease. It is, however, not generally recognized that there exist a considerable number of clinical manifestations which, though often of minor practical importance, yet demonstrate clearly the fundamental nutritional disturbance also present in the Graves' disease. For this reason, the present writer (40) classified some years ago the symptoms on this basis. They are set forth in the following table in more detail:

Classification of the Signs and Symptoms of Thyrotoxicosis
(Janney)

I. *Toxic Signs and Symptoms of Thyrotoxicosis*

Nervous System:

Psychic: Irritability, restlessness, excitability, insomnia, psychoses.

Sensory: Hyperesthesia, pruritus, flashes of heat.

Motor: Tremor, twitchings, trembling, rarely convulsions.

Special Senses: Auditory and luminous phenomena, ocular pain.

Autonomic: Exophthalmos and special ocular signs. Secretory: Sudorrhoea, epiphora, salivation, increased intestinal secretion, etc. Nausea, vomiting, diarrhoea through smooth muscle stimulation. Erythema, purpura, dermatographia, urticaria, transitory oedema.

Cardio-vascular: Tachycardia, cardiac hypertrophy, palpitation, arterial pulsation, functional murmurs.

Respiratory: Tachypnoea, dyspnoea.

Hematopoietic: Toxicity of blood; lymphocytosis, mononucleosis; decreased bacterial alexines.

Metabolism: Loss of weight; increased metabolic rate; excessive breakdown of protein; increased excretion of protein metabolites. Rise of temperature.

Genito-urinary: Toxicity of urine.

II. *Trophic Signs and Symptoms, including those of Thyroid Deficiency and other Endocrine Deficiency*

Thyroid: Hypertrophy, hyperplasia, sclerosis in old cases.

Cutaneous: Atrophy, pigmentation; hair changes (premature greyness, brittleness, alopecia); nail changes (thinness, seaming, brittleness); myxedematous patches; scleroderma. Dentition: premature erosion and caries.

Cardio-vascular: Fatty and sclerotic lesions in myocardium and vessels, myocardial insufficiency, mitral insufficiency, cardiac hypertrophy.

Organic: Various degenerations in somatic organs; albuminuria.

Muscular: Weakness, atrophy, degeneration.

Osseous: Imperfect ossification; thinning and increased fragility of the bones, ununited fractures; rarely osteomalacia.

Metabolic: Delayed glucose assimilation, increase of nitrogenous retention through thyroid therapy, normal or subnormal

metabolic rate in dysthyroid cases.

Ductless Glands: Presence of symptoms and lesions of hypofunctional type referrable to the pituitary (polyuria, polydipsia, fat distribution), thymus (hypertrophy), suprarenals (cutaneous pigmentation, asthenia, diarrhoea), pancreas (alimentary glycosuria, diabetes); lymphatic system (lymphatic hypertrophy, splenomegaly, enlarged tonsils and adenoids); gonads (hypoplasia, decreased libido, dysmenorrhoea, amenorrhoea, menorrhagia).

REMARKS UPON CLINICAL CLASSIFICATION OF SIGNS AND SYMPTOMS OF THYROTOXICOSIS

Many of the trophic changes are of apparent triviality. They are frequently overlooked by clinical observers, perhaps partly on account of the ease with which the diagnosis of thyrotoxicosis can usually be established, merely from the classical toxic symptoms. The cutaneous and blood changes are practically always present and are indeed diagnostic of thyrotoxicosis. The bony lesions are frequent in cases beginning in earlier life. They are not usually observed, as roentgenograms are not often made in these cases. The lesions in the organs are found only at post mortem. Thus Askanazy (51), notes in each case examined widespread fatty infiltration and fatty degeneration of the voluntary muscles. It might be argued on excellent grounds that such lesions are rather of toxic origin, but it will be remembered that similar changes are noted in cretinism and myxedema, so it is preferred to regard them as trophic rather than toxic.

Endocrine Interrelationships in Thyrotoxicosis. As is well known, the condition of hypothyroidism quite often appears in association with hypopituitarism and, indeed, more complex pluriglandular syndromes. If, then, there be clinically observed in Graves' disease accompanying hypofunctional disturbances in other endocrine organs, such may be regarded as additional indirect evidence that a similar, i. e., hypofunctional process, prevails in the thyrotoxic thyroid gland. Such a state of subfunction may thus affect the nutrition of other ductless glands, leading to hypofunctional disturbances in these organs. On the other hand, it is possible that lesions in other ductless glands are due to thy-

roid toxemia or even, in the case of the suprarenals, causative of the thyroid condition (See below).

Occasionally, pituitary lesions are found at autopsy of persons dying of exophthalmic goiter. As emphasized by Hofstaetter (52) and Salmon (53), certain of the trophic symptoms of this disease(see table) may be of pituitary origin. Improvement noted at times on administration of the pituitary preparations would substantiate this view.

Simonds (54) and others have reported hyperplasia and atrophy in the suprarenals in thyrotoxic subjects. The pigmentation and asthenia may be possibly due to accompanying suprarenal involvement. We may, however, not be dealing with cause and effect so far as the possible influence of the thyroid state in Graves' disease on the suprarenal is concerned, for the reverse may be true and adrenal disturbance play a part in the thyroid condition, as suggested by Cannon's researches on the stimulatory effect of adrenalin on thyroid secretion. The recent experiments of Marine and Baumann (55) are of much interest and possible importance in this regard. These investigators found a rise in the basal metabolism to follow injury to the suprarenal cortex in rabbits, accompanied by certain cutaneous and nervous phenomena similar to such found in Graves' disease, but without production of the complete clinical picture. Adrenalin has likewise been shown by Tompkins, Sturgis and Wearn (56), Sandiford (57), and Marine and Lenhart (58) to cause a rise in the respiratory exchange. Removal of the suprarenals causes thyroid hypertrophy. From all this work, it is likely that the suprarenals exert an effect or control on normal, and possibly abnormal, thyroid metabolism. They may thus play a rôle in the etiology of exophthalmic goiter, the exact mechanism of which requires elucidation.

The association of diabetes mellitus and Graves' disease has been reported by various authors [v. Noorden (59), Ewald (60), Falta (61), Sattler (10), 40 cases]. The frequent presence of alimentary glycosuria (many observers) and an increased blood glucose curve [Hamman and Hirschman (62), Geyelin (63), Janney and Isaacson (64)], would suggest a pancreatic affection in Graves' disease. On the other hand, the thyroid itself exerts an influence on carbohydrate metabolism as shown by the de-

velopment of hypoglycemia after thyroidectomy (Janney and Isaacson).

A diffuse adenohyperplasia is regularly found in Graves' disease (Kocher, F. v. Müller). This may include the tonsils, spleen, and intestinal follicles. The lymphoid cell infiltration of the thyroid itself is best considered an expression of the same general process. It is probable that the thymic enlargement, in spite of efforts to bring out a more specific relationship, is but an instance of the general *status thymolymphaticus* present [Capelle (65); see also Eddy's (66) recent review of the literature]. The lymphocytosis and mononucleosis present in both hypothyroidism and exophthalmic goiter are probably due to this *status lymphaticus*. It will be recollected that a similar hypertrophy of the lymphatic system, at times accompanied by thymic enlargement, takes place in hypothyroidism, Addison's and other endocrine diseases.

Signs and Symptoms of Uncertain Etiology. The emaciation and weakness of Graves' disease, though referred to the toxic and trophic group respectively, can be regarded as characteristic of either group. Emaciation is not so uncommon in hypothyroidism. Indeed, the musculature may show definite wasting; weakness can be caused by the toxemia, but again it is one of the earliest symptoms of hypothyroidism. Emaciation and weakness may again be possibly relegated to accompanying suprarenal deficiency.

The cardiac hypertrophy may be compensatory in early cases and due to the tachycardia. It may thus be regarded as a sequela of the toxic stimulation. On the other hand, in cases of goiter heart it may be due to myocardial degeneration which may be either toxic or trophic in origin.

The diarrhoea may, as indicated in the table, be ascribed to toxic stimulation of the intestinal musculature. It may, however, possibly be due to an accompanying suprarenal deficiency or to deficient pancreatic secretion (fatty diarrhoea of thyrotoxicosis).

Certain of the metabolic phenomena ascribed to accompanying endocrine disturbances are of somewhat uncertain etiology. Thus the creatinuria may be due to toxic breakdown of muscle as well as to muscle disintegration due to lack of normal repair and replacement processes.

CLINICAL DYSTHYROIDISM

Aside from the occurrence of the above mentioned thyroid deficiency signs and symptoms in typical cases of Graves' disease, there is a group of cases in which the symptoms of myxedema are frankly intermingled with those of Graves' disease. For this condition the term "dysthyroidism" is particularly applicable, although, for reasons advanced in the present paper, the same designation might well be applied as synonymous with thyrotoxicosis. Usage has, however, restricted the use of this term to cases showing a definite combination of myxedema and thyrotoxicosis.

It is significant that myxedema never precedes thyrotoxicosis, but often follows it. This behavior would be expected from the pathologic and metabolic data already emphasized. Hand-in-hand with the incipient hyperplastic changes are seen the increase in the metabolic rate, protein loss, rise of temperature, and the development of toxic manifestations. As the period of cellular exhaustion, atrophy and sclerosis gradually supervenes, the clinical picture of myxedema slowly develops. On the other hand, cases have been reported by Sollier (67), Jolly (68) and Osler (69) in which the thyrotoxic and myxedematous symptoms occurred simultaneously.

Every experienced internist has observed examples of clinical dysthyroidism which are much more common than usually appreciated, as emphasized by Bertine (70), who reported from the Cornell Medical Clinic in New York, among 133 thyroid cases, 33 cases presenting in no uncertain way a combination of thyrotoxic and hypothyroid symptoms. Thus a combination of tremor, sudorrhoea and at times exophthalmos and tachycardia may be present in patients showing the hypothyroid type of obesity, mental hebetude and asthenia. In surgical myxedema there may likewise be observed typical examples of interposed hypothyroid and thyrotoxic symptoms in which the thyroid remnant left at operation still remains toxic and, in addition, indeed, is functionally deficient through removal of the bulk of the gland. It may be here mentioned that nervousness and tremor are not necessarily always thyrotoxic in origin, as Horsley (71) has observed a nervous excitable stage in experimental athyroidism, and both Horsley (72) and McCarrison (44) have reported such symptoms in incipient myxedema. *The existence of clinical dys-*

thyroidism is a potent argument in favor of the acceptance of the dysfunctional theory. The fact is apparent that both the toxic and trophic symptoms must be caused by morbid processes simultaneously occurring in the same thyroid gland, which lead to the discharge of secretion deficient in quantity but toxic in quality.

THERAPEUTIC EVIDENCE

A real improvement on thyroid medication has been rarely reported in certain cases of Graves' disease and dysthyroidism, particularly those exhibiting marked myxedematous signs (Murray, Dock, *et al.*). This observation has been substantiated by the metabolic studies of Janney (40), as well as Halverson, Bergeim and Hawk (43), who noted an added retention, not a toxic loss, of nitrogen and other protein metabolites on thyroid administration in Graves' disease. This reaction does not occur in control cases. Such observations constitute a demonstration of the normal anabolic function of the thyroid gland in thyrotoxicosis and are of considerable importance as supporting the dysthyroidism theory.

THE HORMONE HYPOTHESIS OF GRAVES' DISEASE

Adherents to the dysthyroidism theory have made various attempts to explain the exact nature of the toxic thyroid secretion. Lampe, Liesegang and Klose (20) accept an altered molecular constitution of the thyroid hormone. In 1918 Janney (40) emphasized that the "hormone hypothesis" supplied a plausible explanation for the complex manifestations of the disease. This view may be quoted in abstract in its original form:

"All evidence tends to indicate that the thyroid hormone is a synthetic product. It is certainly built up by the thyroid from inorganic iodin and other substances possibly related to the indol-containing amino-acid, trytophane. It is possible that one or more of these intermediate substances is toxic, and, indeed, identical with the products arising in the breakdown of the hormone in the body. It is likewise possible that various factors might disturb the normal synthesis of the hormone, the result being the premature discharge of the toxic intermediary product into the circulation. The factors producing this condition might be disturbances in the nervous control of the thyroid metabolism, such as could be produced by fright, emotion, shock or direct organic injury such as trauma, thyroiditis, or again, histologic and gross changes in the parenchyma of the gland; that is, the well known causes of exophthalmic goiter.

"The result of the premature discharge of the hypothetical toxic intermediary product would be an impoverishment of the gland of the thyroid hormone, which would explain the fact that Graves' disease goiters are poor in iodin, and especially in the active alpha-iodin pro-

teins. The decreased production of the normal hormone due to the cause mentioned would tend to be accompanied or followed by the signs of thyroid insufficiency. Thus the deficiency symptoms (Group 2) can be accounted for; also the concomitant occurrence of hypothyroid and hyperthyroid symptoms, and the tendency of exophthalmic goiter patients to develop myxedema.

"The frequent failure of the pathologic picture to coincide with the clinical (see the foregoing) can best be explained by these views, which do not strictly necessitate histologic change at the beginning, but rather a defective endocrine secretory metabolism as the ultimate cause of exophthalmic goiter.

"According to our hypothesis there is present in the thyroid and blood of exophthalmic goiter patients a toxic substance. This view is substantiated by the experiments of Caro, confirmed by Klose, by demonstrating the toxicity of the urine from exophthalmic goiter patients; also recently by Blackford and Sanford, who found a depressor substance in the thyroid and serums of such patients."

R. G. Hoskins (73) and C. P. Howard (7), among others, have favorably regarded such an hypothesis. Plummer (38) followed by Boothby (38), incline recently to the same viewpoint, the latter erroneously ascribing it to Kendall.

However desirable it is to discard the time-worn "hyperthyroidism" for the "dysthyroidism theory" it seems timely to remark that the "hormone hypothesis" is lacking in proof which must include the isolation and identification of a thyrotoxin, chemically related to thyroxin. In the present meager state of our knowledge, this hypothesis is merely deserving of recognition as a working idea for the stimulation of further studies in the difficult field of thyroid research.

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THE POSITIVE ACHIEVEMENTS OF ENDOCRINOLOGY

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The recent appearance of a number of hypercritical articles on endocrinology tends to create a state of unwarranted skepticism toward this branch of medicine. So much stress has been laid upon the negative accomplishments that it is not amiss to present a brief review of its positive achievements.

From the standpoint of the clinician all investigations center toward one object: progress in diagnosis and in therapy.

While attending a large medical meeting recently, the writer was impressed by the negative tone that dominated most of the papers submitted. So much was said of what had *not* been accomplished and so little stress was laid upon what *could* be accomplished in therapy, that most of the physicians took back with them a mass of unknowns with which to combat their perplexing daily problems.

It is distinctly desirable to maintain a critical attitude toward anything new in medicine, and such an attitude is an excellent balance to the unwarranted claims of many misguided enthusiasts. However, there has been so much progress made in many branches of medicine within recent years that it is of prime importance to call the positive achievements to the attention of the medical profession, and to place the new facts in the hands of the general practitioners to strengthen their armamentarium in the diagnosis and treatment of disease.

The interested practitioner who studies endocrine literature is bewildered by the combat between the enthusiasts and the conservatives. It is most unfortunate that so many extravagant claims for endocrine therapy have been made by certain mercenary manufacturers of organic products. To them most of medicine is endocrinology and they supply the physician with ready-made formulae for the cure of every disease or condition that flesh or mind is heir to. Furthermore, the suggestiveness of the positive facts and the large number of unknowns in endo-

crinology stimulate the imagination. This has led to literary outbursts of enthusiasm which present certain suggestions and probabilities as established facts.

For the past five or six years, the writer has conducted a clinic for the systematic study of medical problems from an endocrine standpoint, making as careful clinical and laboratory observations along these lines as facilities permit. This work has demonstrated that this branch of medicine, in spite of its shortcomings, has made positive contributions to clinical medicine.

In order to judge of the progress of any branch of medicine we must take into account the age of the subject and compare its achievements with those of other branches of medicine. Endocrinology dates as such only from 1889, but in this brief period it has made progress proportionately greater than any other branch of medicine.

Although conversant with the experimental and laboratory literature, being primarily a clinician, I shall confine myself principally to the contributions made to clinical medicine, to therapy, and to public health medicine.

We may divide the progress in endocrinology into several categories: (1) progress in the well-established syndromes of the various ductless glands; (2) contributions of endocrinology toward various non-specific branches of medicine; (3) contributions to therapy, and (4) contributions to public health. In the definite syndromes I shall discuss only the generally recognized ductless glands.

DEFINITE CLINICAL SYNDROMES

The thyroid syndromes were to some extent appreciated in 1850, when Curling first described cretinism. This was followed, in 1873 by the description of myxedema, by Sir William Gull. In 1882, Reverdin showed that the complete removal of the thyroid produced myxedema—while in 1888, only thirty-four years ago, Sir Felix Semon grouped all the various facts about the thyroid and proved conclusively that cretinism, myxedema and post-operative myxedema are due to the same cause—thyroid deficiency. In 1891, Murray, a pupil of Sir Victor Horsley, presented the first case of myxedema treated successfully by oral administration of thyroid extract. The effect of this communication was far reaching because it not only established a cura-

tive therapy for myxedema, but it established the therapeutic principle that, given a deficiency of a certain incretory gland the oral administration of a dried extract of that organ can be curative.

The description by Graves in 1835, by Parry, 1786-1815, by Flajani, 1802, and by Basedow in 1840, of the syndrome of exophthalmic goiter was followed by the work of Kocher, who demonstrated that partial thyroidectomy could cure exophthalmic goiter. And thus was established the surgical treatment of exophthalmic goiter, which later came to include the use of thyroid vessel ligation, either complete or preliminary, by the Mayo Brothers, and the perfection in technique in the surgery of the thyroid, by Crile. The contrasting syndromes of myxedema and cretinism, and exophthalmic goiter, led to the conception of two disturbances of function in the ductless glands: hyper-activity and hypo-activity, one being regarded by many as evidence of over-activity and the other evidence of under-activity.

In 1915, Hertoghe (and later Levi and Rothschild) described clinical conditions in which thyroid deficiency occurred in a very mild form—the so-called *forme fruste*. *Forme fruste* types of over-activity of the thyroid have also been described, but since many of the symptoms of this type of disturbance occur in various neurotic conditions, it was largely a matter of judgment as to whether, in the absence—or even in the presence—of an enlargement of the thyroid gland, the physician was dealing with a condition of neurasthenia or of hyperthyroidism.

Boothby, Aub and others, a few years ago, however, established the fact that an increase in the basal metabolic rate, in the absence of fever, is nearly always an indication of hyperthyroidism and that the degree of apparent hyperthyroidism is in proportion to the increase in the basal metabolic rate. This important fact, while generally accepted in clinical medicine, is of comparatively very recent date.

Still more recent is the isolation of thyroxin, a definite hormone, by Kendall of the Mayo Clinic, and the demonstration of its effect on metabolism.

The etiology of hyperthyroidism, however, is still in doubt. The question as to whether nervous influences initiate the condition, or whether the hyperthyroidism is behind the nervous element has not yet been settled. There is some evidence, also, that

other ductless glands may play an important rôle, either primary or contributory, and that infections and diet are important factors. The differential diagnosis of hyperthyroidism from states of autonomic imbalance and the relation of hyperthyroidism to basal metabolism have been much discussed. This discussion seems due largely to the geographical location of the cases: the frequency of endemic goiter in iodine-poor districts; and the greater frequency of autonomic imbalance in urban districts.

In the etiology of thyroid deficiency more progress has been made. The work of McCarrison in producing goiter in animals by administering fecal matter threw some light on the subject. Subsequently, Marine made the clinically important observation that the absence of iodine in the food or drinking water is a specific factor in the causation of endemic goiter. Furthermore, he and others proved that by increasing the iodine content of the food or the water endemic goiter could be made to disappear.

Pituitary Syndromes. Pituitary syndromes were first recognized in 1887, when Minkowski described acromegaly. In 1889, more extensive contributions by Pierre Marie established this syndrome, while, in 1886, Sir Victor Horsley cited experimental evidence that the pituitary is necessary to life, though this statement has been controverted by Aschner. In 1908, Paulesco, of Bokhara, removed the pituitary gland; while in 1911, Cushing, in his memorable monograph, reported evidence that the adiposo-genital syndrome of Froehlich is due to a pituitary deficiency. This was followed by the cure of diabetes insipidus by injections of pituitrin. Furthermore, it is evident, on clinical examination, that in diabetes insipidus the patients show evidence of pituitary disease. Lately, a report has been made, by Blumgart, that the same results could be obtained in diabetes insipidus by spraying the pharynx with pituitrin as by hypodermic injections. Although in recent years the glandular origin of diabetes insipidus and of the Froehlich syndrome has been questioned by Bailey and Bremer, Camus and Roussay, and others, the suggested origin being a lesion in the tuber cinereum; the efficacy of pituitrin, however, has not been questioned. There have also been some encouraging reports of the results of treating diabetes insipidus by dried extracts. It must be remembered that all these are facts of very recent origin.

The work of Cushing has taught us to recognize pituitary

tumors. It has further taught the various manifestations of pituitary disease. It has called attention to syndromes similar to those of a pituitary tumor without the eye symptoms, such as pituitary headache and the various forms of pituitary syndromes; it has suggested a possible endocrine (pituitary) origin for epilepsy. Furthermore, the study of typical pituitary syndromes indicates the frequency with which this condition occurs. Englebach has supplied a masterly classification of pituitary diseases which has helped to clarify the various syndromes.

The therapy of pituitary syndromes, while it has as yet distinct limitations, has demonstrated definite results. These conditions have been accurately described only within the past ten years and the recognition of the syndromes have resulted in operative procedures on pituitary tumors, with notable results or the relief of the conditions by x-ray therapy. Progress in other forms of treatment of pituitary syndromes has been made, such as the use of pituitary extract in alleviating the so-called pituitary headaches and the abdominal crises. We have, however, been unable to influence by therapy such conditions as acromegaly. Although reports of reduction in weight, and acceleration of genital development, in pituitary syndromes have been made, these are still questionable for, in many of the instances, the genital development is merely a retarded puberty and, in my experience, weight reduction by pituitary extracts is still an unsolved problem.

Disturbances of the Adrenals. Disturbances of the adrenal glands were really recognized by Addison in 1855. Since then various minor grades of Addison's disease have been described. Since injury to the adrenals—as by hemorrhage or infections—produces symptoms similar to those of a mild Addison's disease, it is believed, on clinical grounds, that a condition of adrenal insufficiency occurs in various infections and in neurasthenia. This statement has been questioned by experimental physiologists because of their inability to reproduce the condition in animals. The work of Cannon on the discharge of adrenalin in emotional and psychical states has been of tremendous importance in establishing a definite physiologic status for the adrenals, although it has not been, as yet, of very great clinical value. The recognition and description of adrenal tumors, as well as the description

by the French of the condition known as "virilism," is a definite contribution to clinical medicine.

The adrenal cortex has been shown to be extremely important in physiologic processes; indeed, it is pretty definitely established that the adrenal cortex is essential to life. The recent work of Marine and Baumann indicates the importance of the adrenal cortex in heat production and respiratory exchange and suggests its rôle in hyperthyroidism, though the work still needs corroboration.

The Thymus Gland. With regard to the thymus gland the progress has been comparatively slow. It is definitely established that the thymus persists throughout childhood and disappears in adolescence. It is enlarged in hyperthyroidism. It is enlarged in cases of status lymphaticus. It produces certain respiratory symptoms in childhood. It is enlarged in certain forms of acute lymphatic leukemia. Certain tumors may arise from it. However, clinical study of cases with persistent thymus shows that thymic patients frequently develop pituitary syndromes and mild grades of the so-called Addison's syndrome. Such patients very often have small hearts and small blood vessels. Timme has studied the compensatory mechanism seen with the persistent thymus.

The Pineal Gland. Quite recently, attention was called to the disturbances of the pineal by Frankl Hochwart, in his description of a case of precocious development of the genitals. In 1907 Bailey and Jelliffe collected about twenty-seven cases of this syndrome. This has taught us to recognize this lesion by the presence of an ophthalmoplegia interna, and precocious puberty. The precocious mental development of Frankl Hochwart's case has led to much speculation about the rôle of the pineal in mental deficiency, but the reports of therapy along these lines must still be considered critically.

The Gonads. That the gonads have an internal secretion was proved definitely by Berthold, in 1849, by showing that the secondary sexual characteristics of cocks disappeared when the testes were removed, but not when the external duct or the nerves of those organs were interfered with. The artificial production of eunuchoidism, a procedure carried out from time immemorial, also demonstrates that the genital organs are responsible for the secondary sex characteristics. The work of Tandler

and Grosz on eunuchoidism indicated the important rôle in growth and development and in psychical manifestations of the genital organs. Lydston showed, years ago, that he could transplant testes successfully. Recently Steinach has been able to produce masculine characteristics in female guinea pigs by removal of the ovaries followed by transplantation of testes, and female characteristics in male guinea pigs by removal of the testes followed by transplantation of ovaries. Furthermore, he was able to produce hypertrophy of the interstitial tissue of the testes by ligation of the ducts, thus establishing an important method in endocrine experimentation.

The Ovaries. With the advent of aseptic surgery and the frequent removal of diseased ovaries a great deal was learned about the physiology of these organs. While it is comparatively easy to recognize syndromes of ovarian deficiency by the absence of secondary feminine characteristics and by menstrual disturbances, it has not been so easy to recognize specifically syndromes of excessive activity of these glands. The importance of the corpus luteum in menstruation has been established. And there is a good deal of evidence which indicates that other ductless glands participate in ovarian function.

The Pancreas. The fact that the pancreas has an internal secretion, probably originating in the islands of Langerhans, requires no proof at the present time. All our clinical and experimental knowledge of diabetes mellitus belongs to endocrinology. The recent work at the University of Toronto, where a substance, "insulin," which is capable of reducing hyperglycemia, has been prepared from the islands of Langerhans, seems to mark an important step in advance. Recently, also, the fact that Friedman was able to reduce hyperglycemia without producing myxedema after partial pancreatectomy by ligation and partial removal of the thyroid, suggests that in sugar metabolism, ductless glands other than the pancreas play an important rôle. Both of these facts are exceedingly important.

The Parathyroids. Parathyreoprivic tetany is well known. McCallum showed that the injections of calcium salts would relieve tetany. Parathyroid administration for tetany has often been tried, but with questionable results. The recent work at Carlson's laboratory indicates that parathyroid removal produces tetany only in the presence of protein putrefaction, in the

intestine. This seems to indicate, at least for the parathyroid, that it functionates not by producing hormones, but by detoxication.

Glandular Interrelationships. There is considerable evidence of glandular interrelationship, both from the clinical and laboratory sides, although laboratory experiments have until recently been unable to prove such relationship conclusively. We have evidence of a pituitary and thyroid relationship, of a thyroid and adrenal relationship, of an adrenal and a pancreatic relationship, of a thyroid and parathyroid relationship, of adrenal and gonad relationship, and a gonad and thyroid relationship and a gonad and pituitary relationship. Experimentally, however, Marine has recently shown that freezing the adrenal cortex increased the basal metabolic rate and hence perhaps affects the thyroid. His later work has shown an adrenal cortex and gonadal relationship. The explanation of these relationships on the basis of metabolic changes is untenable nor does it vitiate its endocrine mechanism. Friedman's work on a thyroid-pancreas relationship has been previously mentioned. The literature contains a vast mass of scattered data on such relationships.

ENDOCRINOLOGY IN MEDICINE

The greater importance of endocrinology lies not so much in the recognition of the various specific syndromes as in its contributions to other branches of general medicine. There is hardly a phase of medicine in which endocrinology does not play a rôle. The profound lethargy and the lack of initiative of the Addison syndrome, the hyperexcitability of the hyperthyroid syndrome, the sluggish mentality of the myxedematous individual, the hyperexcitability and abnormal fears in exophthalmic goiter, the lack of initiative and psychical monotony of the eunuchoid, all indicate the important rôle of the ductless glands on the nervous system. The increased metabolic rate of hyperthyroidism and its diminution in myxedema and in cretinism; the obesity of the pituitary syndrome and of the menopause, all demonstrate the profound influence of the ductless glands on metabolism. Apart from the definite syndromes we may recognize endocrine manifestations in clinical medicine, principally as disturbances of development and disturbances of physiology.

The appreciation of disturbances in development is com-

paratively new, and a great deal still remains to be accomplished, but there are certain positive data that have been contributed by endocrinology.

1. We can recognize real cretinism and juvenile myxedema as causative factors in disturbances of growth and development in children.

2. We have evidence of pituitary syndromes as causes of disturbance in development, such as the Froehlich syndrome and the Lorrain-Levi syndrome with its adiposity, its changes in bony growth and its delayed puberty, or partial or complete genital atrophy, and its increased sugar tolerance accompanied frequently by diabetes insipidus.

3. In older children, we have evidence of disturbances as the result of genital deficiencies. The close relationship in bony growth between the pituitary and the gonads is an important factor in the recognition of disturbances of growth.

4. We have evidences of retardation in mental development, in association with thyroid deficiency, and in association with gonadal deficiencies.

5. In a number of disturbances of mental development as in various forms of idiocy, there is clinical evidence of pluriglandular disease. But the specific glandular disturbances in these cases have not been worked out. There are encouraging reports in the literature of the treatment of these cases by organotherapy, but the results are as yet by no means uniform.

ENDOCRINE ORGANS AND THE TEETH

A good deal of importance has been placed on the character of the teeth as evidence of endocrine disturbance. We may note large upper front incisors; increased spacing; overcrowding of the teeth; absence of, or rudimentary, upper lateral incisors, as evidence of gonadal deficiency; large or rudimentary canines as evidence of an adrenal disturbance; early decay of the teeth.

The increased spacing is the most definite characteristic and simply indicates enlargement of the cranial bones and associated large pituitary. Overcrowding apparently suggests the reverse. The deficiency of the upper laterals, the significance of which is still undecided, seems to indicate certain gonadal developmental disturbances. These observations need statistical corroboration. There may be a basis for these conditions of the teeth. There is

apparently a regularity in the order in which the teeth appear and abnormalities of development of the teeth may indicate a retardation or disturbance at a specific stage of development. The subject offers a fruitful field for systematic investigation.

DISTURBANCES IN PHYSIOLOGY

Until very recently the major part of the medical student's course has been devoted to the clinical recognition of pathology, and the patient unfortunate enough not to have a recognizable lesion was usually regarded as unworthy of the serious attention by the average medical man. It is inconceivable that functional change should be manifest without structural change, but it is possible to have functional changes without appreciable structural change. While we are awaiting the recognition of the pathology of many diseases we must content ourselves with the recognition of abnormal physiology. Since the incretions are important factors in modifying function and perhaps in controlling function, the appreciation of the rôle of the ductless glands in any disease is of importance in those diseases where our present methods do not recognize a pathological basis. Thus, as a working hypothesis, we may say that the thyroid regulates the speed of metabolism, and possibly of function, the adrenals possibly modify the vigor of function, and the gonads may give character to function. But aside from these rather philosophical conceptions, endocrinology has contributed a great deal to the recognition and the treatment of functional disease.

From the group of the unknown so-called functional diseases, endocrinology has taught us to recognize certain distinct syndromes.

1. The recognition of myxedema by a low basal metabolic rate as a cause for joint pains, for gastric symptoms, for drowsiness, etc.

2. The recognition of mild grades of hyperthyroidism, with visceral or abdominal crises, with nervous symptoms, by means of basal metabolism determinations. The recognition of cardiac-neuroses, as evidence of hyperthyroidism, recognized by the application of basal metabolism studies.

3. The recognition of functional pituitary syndromes which has followed the recognition of pituitary tumors. The characteristic pituitary headache, with abdominal cramps, visceral

crises, gastric and uterine crises, dysmenorrhoea, migraine, and, possibly, epileptiform attacks.

4. The appreciation that gastric neuroses have apparently a constitutional basis; the appreciation that the increase in or diminution of the acidity is not a clinical entity, but a constitutional dyscrasia; the fact that such crises occur in hyperthyroidism indicates that the thyroid and the adrenals may play a rôle in these conditions; it is possible that an ulcer may be a terminal state of this condition. The frequent occurrence of duodenal ulcers after severe burns, and the demonstration of hemorrhages into the adrenals in these conditions as well as the work of Rogers on the effect of thyroid and suprarenal nucleoproteins on the nerve terminals of the stomach strongly suggests an endocrine factor.

These are some of the contributions that endocrinology is making toward progress in clearing up very common apparently functional conditions.

A few years ago, Eppinger and Hess called attention to constitutional states characterized by disturbance in the balance of innervation between the parasympathetic and the sympathetic branches of the autonomic nervous system, which they have grouped as states of "vagotonia" and "sympathicotonia." The frequent occurrence of these states in various syndromes of the ductless glands, particularly in hyperthyroidism, suggests a relationship of these conditions to the latter syndrome. Practically, however, it is very rare to find a pure state of vagotonia or of sympathicotonia. These constitutional syndromes do exist, but not in the well-defined groups as described by Eppinger and Hess; they are characterized by extreme variability, vagotonia existing at one time and sympathicotonia at another; or both existing together. The patients very frequently have many of the symptoms of what are ordinarily called mild grades of hyperthyroidism. The differentiation, however, can be made by a basal metabolic determination; whether hyperthyroidism is the result of autonomic imbalance or whether the reverse is true is still an open question. Rogers has been able to produce the gastric symptoms of autonomic imbalance by the injection of thyroid and suprarenal nucleoproteins. Other experimenters have obtained negative results, but the question must still remain open.

Endocrinology has made a contribution to the clinical knowledge of obesity, for, on the basis of definite endocrinopathies it is possible to recognize different types of obesity, such as the generalized, the epigastric, the lower abdominal, the trochanteric obesity, and obesity confined to the lower extremities.

Endocrinology has also fostered an important branch of medicine which we may term constitutional medicine or medical anthropology. The individual differences of people, their physiological and anatomical variations and their singular reactions to disease have been claimed to be due to the domination of certain ductless glands in their growth and development. This is a fruitful field for investigation and much stress has been laid upon this work by Sir Arthur Keith. At any rate the recognition of the pituitary syndrome of Froehlich, the Lorrain-Levi syndrome, as well as the description of the characteristics of the eunuchoid, by Tandler and Gross, has demonstrated that numerous individuals exist who apparently suffer little but who show the anatomic makeup of the Froehlich syndrome, the acromegalic, and the eunuchoid. The accurate descriptions of the various manifestations that result in such people has indicated that they may suffer from various functional disturbances on the basis of their singular makeup. Individuals with persistent thymus have also been described, with singular secondary characteristics as the result of their compensations. This is a branch of medicine which is still in its infancy, but it is a contribution of endocrinology which promises progress in certain functional diseases and especially in gynecology. Whether it holds realities or not only time and accurate studies will tell. It may help to solve individual reactions in disease.

ENDOCRINE FACTORS IN NEUROLOGY

The psychical changes and the changes in the physiology of the nervous system, such as the abnormal fears and excitability of hyperthyroidism, the sluggish mentality in myxedema, the lack of psychical initiative in eunuchoidism, the psychical manifestations of the over-sexed and the under-sexed, the psychical manifestations during menstruation, pregnancy, and at the menopause, etc., the relationship between the ductless glands and states of autonomic imbalance, all indicate the close relationship

between the ductless glands and the nervous system. It is also apparent that there are distinct psychical sex differences in the psychological manifestations of individuals and, although such conditions are apparent in every day life, they are not subject to laboratory proof, nor are they even subject at the present time to accurate psychological measurement. There are no psychological tests to differentiate a male from a female nor are there any reliable tests to measure the emotional states of individuals. These are all problems begging for solution.

Practically, however, certain pathologic changes have recently been described in the testes in cases of dementia praecox. There is also an apparently basic endocrine cause in the psychoses of pregnancy and post-partum states.

The occurrence of symptoms resembling Addison's syndrome has suggested that the adrenals are a factor in neurasthenia, but this has not been corroborated by laboratory proof. At any rate, it has proved a basis for organotherapy.

Homosexual tendencies and sex abnormalities suggest a ductless gland basis.

The Freudians are beginning to appreciate that the constitution of the patient is important in the psychology of the subconscious.

ENDOCRINE FACTORS IN GYNECOLOGY

The appreciation of the known facts in endocrinology is of prime importance to the gynecologist. Gynecological physiology largely constitutes the physiology of the ovaries, as well as the other ductless glands. Menstruation, ovulation, pregnancy and the menopause are due to definite physiologic processes of the ovaries, in which other ductless glands partake, hence it is essential for the gynecologist to be thoroughly familiar with endocrinology. The physiology of menstruation is not definitely known, but we do know that it is dependent upon the physiology of the ovary, probably the corpus luteum. The corpus luteum prepares the uterine endometrium for pregnancy, but when no pregnancy takes place the endometrium degenerates and menstruation occurs. Many gynecologists deny the participation of other ductless glands in the physiology of menstruation or in the physiology of the ovaries, but there is abundant evidence to the contrary. For example: the occurrence of amenorrhoea in a pituitary tumor, and in the Froehlich syndrome, the occurrence

of amenorrhoea in hypothyroidism, the presence of dysmenorrhoea in pituitary disease, the occurrence of headaches similar to those present in pituitary tumors, at the menstrual period, the occurrence of hyperthyroid symptoms and the basal metabolic changes which have been described, at menstruation, all indicate a participation of other ductless glands in the physiology of the ovary. The ductless glands play an important rôle in the physiology of pregnancy, as is indicated by frequent enlargement of the thyroid, disturbances in metabolism, and obesity. Difficulties in labor also arise from abnormalities in development resulting from preadolescent disturbances of the ductless glands, such as the masculine type of pelvis and the infantile uterus, of the Froehlich syndrome. Gynecology has until recently been dominated largely by mechanical conceptions and the mechanical conditions of the uterus and ovaries on examination or found at operation are utilized to explain symptoms such as sterility and functional menstrual disturbances. Patients are curetted for these conditions without any benefit, when an infantile uterus (part of a constitutional Froehlich syndrome) is the cause. It is essential, therefore, for the gynecologist to recognize endocrinopathies in conjunction with his work, for sterility may be due to hypothyroidism, to an infantile uterus—part of the genital atrophy of the Froehlich syndrome; amenorrhoea may be part of the Froehlich syndrome or part of hypothyroidism, or of a primary genital atrophy which can be recognized by its secondary skeletal changes. The obstetrician must recognize that a masculine type of pelvis, occurring in pituitary syndromes, the result of a pituitary deficiency, may produce obstruction in labor and that the Froehlich type of patient may suffer from uterine inertia during labor.

The differentiation of the type of patient, so far as we know it at present—the eunuchoid, the pituitary and the thymic types with their secondary thyroid manifestations—is important in explaining functional menstrual disturbances. The menstrual disturbances in adolescence or in endemic goiter is another contribution endocrinology has made to gynecology. The menstrual disturbances occurring in autonomic imbalance are also important in the appreciation of functional gynecological disturbances.

Although these conditions are apparent, it is merely the

beginning of the positive contributions that endocrinology promises to gynecology. This does not necessarily mean that gynecology is now simplified and that all symptoms will respond at once to organotherapy, but it is a great step forward to the real biochemical appreciation of gynecological physiology. It is an advance from the mechanical conception, where a tilted uterus is made to account for sterility or for all symptoms. The appreciation of the constitutional factors in gynecology suggest organotherapy, but its value in gynecological disturbances must be determined entirely on its merits.

THE CONTRIBUTIONS OF ENDOCRINOLOGY TO PUBLIC HEALTH AND EUGENICS

In the short time that acute interest has been aroused in this branch of medicine, a few definite contributions have been made in the field of endocrinology to public health medicine. Marine demonstrated that endemic goiter is due to an iodin deficiency and he established a means for its prevention by placing iodin in the water supply, and the administration of iodides in various forms by mouth in goitrous districts. Iodine table salt is now commonly used in the middle west, as suggested by Hirschfelder, and in Switzerland iodized chocolate, for the prevention of endemic goiter.

It has not been generally appreciated that the recognition of the Froehlich syndrome and congenital eunuchoidism are often accompanied by permanent sterility and that the subjects should be advised against marriage. There are no greater marital tragedies than those of the over-sexed married to the eunuchoid or to the pituitary type with genital atrophy. But before advising such individuals one must be sure that the sterility is permanent. Occasionally the genital deficiency may improve after a normal sexual life incident to marriage.

TREATMENT OF ENDOCRINOPATHIES

We may divide the progress made in the treatment of endocrinopathies into surgical and medical therapy. Surgical therapy has given good results in thyroid disturbances, partial thyroidectomy for goiters and partial thyroidectomy or ligation of the superior thyroids for hyperthyroidism. The removal of pituitary tumors in the hands of such men as Cushing and Frazier, who have developed the most perfect technique, gives brilliant

results, and the medical profession is greatly indebted to them for their efforts to teach the recognition of these conditions. The discussion of surgical therapy on the testes and ovaries requires no comment. Recently there have been reports of successful results from testicular transplantation at the hands of Lydston and others, but the results are still questionable. The Steinach operation has been claimed to be successful as a means of stimulating the interstitial tissue of the testes for premature senility, but the results must still be considered critically. There has also been reported successful results following removal of one of the adrenals in epilepsy, but the results are still variable.

ENDOCRINE ORGANS AND X-RAY THERAPY

The x-ray and radium are powerful means of treating disturbances of the ductless glands. Practically the best results have been reported in the reduction of a large thymus, and in exophthalmic goiter. X-ray and radium applications to the pituitary, following operations, have also been more or less successful.

ORGANOTHERAPY

The establishment of the syndromes of hypo- and hyperactivity has led to the establishment of the hormone theory of ductless gland physiology. While it is apparently true that in many instances the discharge of a substance into the blood stream is the modus operandi of some ductless glands, this may not be true of all. Some of the ductless glands may act by detoxication, or by means as yet unknown. However, the hormone theory has established a basis for organotherapy. No matter what other explanations for organotherapy may be offered they are as yet largely theoretical and at the present time, when this form of therapy is efficient, it is substitution therapy; that is, if there is a deficiency of substances in the body that are normally supplied by a ductless gland that is diseased, this deficiency may be overcome by administering an extract of a corresponding normal gland. This has been definitely established in the case of myxedema when definite objective results are obtained by thyroid therapy. The fact that such specific results could be obtained led to the rational assumption which may or may not be true, that, given a deficiency of other ductless glands, similar results could be obtained. The proof of this assumption,

however, can only be established by actual trial in a sufficiently large number of cases under properly controlled conditions. Although the extracts of other glands have been used extensively it is most unfortunate that there is no satisfactory statistical study of any of them. However, certain definite results have been obtained with organotherapy, although there are also a large number of failures. The explanation of these failures may be that the underlying basis for such therapy does not apply to all glands, or that some products as they can be prepared today are not efficient. Progress along these lines can be made by establishing a new underlying basis or by the preparation of products that will be more efficient. We can summarize, however, the actual accomplishments in organotherapy at the present time.

1. Thyroid extract is a specific remedy for thyroid deficiency. Thyroxin, given intravenously, is a much more potent and more definite substance.

2. Pituitary therapy is indicated in states of pituitary deficiency, such as the Froehlich type or the Lorrain-Levi type. Practically, we have dried extracts of pituitary, anterior lobe and whole lobe, and pituitrin, the extract of the posterior lobe. Pituitary extracts have a limited value in pituitary syndromes. It is impossible to modify the physical manifestations of the pituitary syndromes by the use of pituitary extracts; it is questionable whether we can modify the obesity of the Froehlich syndrome in spite of the fact that reports of such results occur in the literature. It is also, probably, impossible to modify the genital deficiencies of the Froehlich or other pituitary syndromes. There are reports of success in this regard in the literature, but these are largely in adolescent children where spontaneous improvement in genital development occurs, since the genital deficiency in the successful cases was merely a retarded puberty. However, definite results can be obtained by the use of pituitary extracts for the relief of the characteristic pituitary headaches, and in some instances relief of the associated symptoms, such as the abdominal visceral crises, and the amenorrhoea and dysmenorrhoea, which are the other manifestations of pituitary disturbances. We should not minimize the importance of these results for the patients afflicted with pituitary disease other than tumor suffer largely from these symptoms apart from the

adiposity and the genital disturbances. The adiposity often responds to dietetic therapy, whereas the genital deficiency may be temporary, slight or permanent, and in the latter instance is not as a rule amenable to therapy. Good results have also been reported in epilepsy, but with the well-known variations in the frequency of the attacks, and the response of epilepsy for a time to other forms of therapy, it would be best to hold these results in abeyance until statistical data with proper controls can definitely establish them.

Pituitary therapy is occasionally useful in modifying the menstrual disturbances incident to pituitary deficiency, such as amenorrhoea.

The dosage of pituitary extract is variable. Since we are attempting to supply an apparent deficiency of some substance in the body and since we have no way of measuring this deficiency quantitatively, we do not know the dosage. Practically, there is a marked variation in the quantities necessary to produce the effects that are possible to obtain, some patients requiring very small doses and others requiring enormous doses. Furthermore, there is a sex difference in the effect of pituitary therapy: female patients respond more readily than male.

The use of dried ovarian extracts is one of the most common forms of organotherapy. I venture to say that most gynecologists use this repeatedly in practice with a definite assurance of results. It is logical to use this substance in the menopause, which is evidently due to ovarian deficiency, and especially in the artificial menopause. There are no adequate statistical data as to the actual results. Desiccated corpus luteum is probably more valuable. In large doses it is useful in checking the vomiting of pregnancy. The intravenous use of corpus luteum extracts also gives definite results. The intravenous administration of ovarian extract and corpus luteum extract is distinctly useful in checking the nervous and psychical symptoms which are common at the menopause.

Organic products are useful in functional disturbances of menstruation when we can recognize a deficiency clinically: a thyroid deficiency indicates the use of thyroid extract, a pituitary deficiency indicates the use of pituitary extract, but the results in functional gynecological symptoms where a specific deficiency cannot be recognized are not so definite. Judgment

as to the efficacy of ovarian and corpus luteum extracts in functional menstrual disturbances must still await controlled statistical data.

Adrenal cortex is a remedy which has recently been introduced for hyperthyroidism, based on the fact that it has been demonstrated that an increased metabolic rate results from injury to the adrenal cortex. While the results of this form of therapy are distinctly encouraging, it still awaits statistical proof.

The use of orchic and testicular extracts is logical in the symptoms of premature senility in males—what we might term the masculine menopause—and in frank eunuchoidism. But the actual effects of these substances must still be regarded very critically in spite of the fact that the specific deficiency is rather easy to recognize.

The use of thymus extract is still in the experimental stage and the same may be said for pineal extract.

Parathyroid extract is in common use, but we cannot as yet state whether it produces definite results or not. The latest work on the physiology of the parathyroids seems to indicate that their function is not hormone production, and consequently, the administration by mouth of parathyroid extract may not prove useful.

PHARMACEUTICAL PRODUCTS OBTAINED FROM THE DUCTLESS GLANDS

Within the past two decades, there have been isolated a number of specific substances from the ductless glands: adrenalin from the adrenal medulla and pituitrin from the posterior lobe of the pituitary gland. These substances produce unquestionable and definite pharmaceutical effects. Adrenalin is a powerful vasoconstrictor; it is able to relieve specific attacks of bronchial asthma, and recently it has been demonstrated that injections of adrenalin relieve the cramp-like pains of gastric ulcer. Pituitrin is a powerful uterine and involuntary muscle stimulant; it is a specific for diabetes insipidus. The pharmacologic effect of these substances has led to the deduction that they are secreted into the blood stream. While we have no such positive proof, it is distinctly justifiable to assume that similar substances, or mother substances, may be present in those glands

which produce such effects in the normal physiology of the individual.

Thyroxin is an important and potent substance which has recently been isolated from the thyroid gland and produces powerful and definite effects in thyroid deficiency and is capable of elevating the basal metabolic level. The recently described substance insulin, which was obtained from the islands of Langerhans of the pancreas, has been shown to reduce diabetic hyperglycemia both in dogs and men.

The use of placental, mammary and other extracts is still in the experimental stage.

PLURIGLANDULAR THERAPY

It is apparent that in many endocrinopathies there is evidence of disturbance in more than one ductless gland, and in many instances there is evidence of pluriglandular deficiency. Nevertheless, it seems to me highly unscientific to prepare shotgun combinations of gland substances in the hope that the body will extract from these combinations those that it needs. The only way progress will ever be made in rational organotherapy is to be able to recognize specific deficiencies and to supply effective substances for these deficiencies. If more than one deficiency is present they should be individually recognized and two or more corresponding substances given.

While organotherapy still has definite shortcomings, it has, nevertheless, established the substitution principle of therapy. It has developed, within two decades, possibly five distinct new and reliable therapeutic agents. Several others give sufficient promise to warrant careful study.

But organotherapy is by no means unique in its shortcomings. The literature on therapeutics in general is remarkable for the paucity of systematized, controlled data on the efficacy of even the simplest remedies. The iodides, the bromides, the salicylates, and the vast group of coal tars, are used daily to the extent of tons, and the only effects obtained are for the large part subjective.

With the exception of the advances made in specific bacteriocidal and antitoxic therapy, progress in drug therapy has lagged. With the past two decades the only major advance has been the development of salvarsan and arsenic preparations,

which are distinctly useful in the relief of the first and second stages of syphilis and the specific gummatous syphilitic condition of the third stage. The effects on syphilitic endarteritis, aortitis, or aneurysm, paresis or tabes, give problematical subjective results, and very little, if any, objective result. Yet no one questions the use of antiluetic treatment for these conditions. Similarly, in the pituitary deficiencies it is logical to use the best preparations of pituitary extract that we have at hand, and although it is rare to get a marked objective result, it is, however, possible in a very large percentage of the cases to obtain relief of the symptoms that the patients actually suffer from. Such therapy is harmless and is far less deserving of criticism than the use of poisonous coal tars with the sole object of relieving subjective symptoms.

CONCLUSION

I have attempted to summarize the positive contributions that endocrinology has made to clinical medicine. Special limitations preclude covering the entire field, and I have attempted to present only the outstanding facts. I have stressed the positive findings because the negative findings have been so thoroughly stressed by others. I am quite conscious of the shortcomings of endocrinology, but these are merely in line with the shortcomings of medicine in general. They are not specific for endocrinology. The future of endocrinology is pregnant with progress, but it requires careful and critical study by investigators interested only in the search for truth. The opportunities for investigation lie both in the clinic and in the laboratory. As Dr. Barker has pointed out, in his chairman's address at the symposium on endocrinology at the last meeting of the American Medical Association, some laboratory workers seem to think that their field alone can develop truths and that the clinician can only develop errors. It must be borne in mind, however, that there are just as many possibilities for error in the laboratory as in the clinic. Laboratory experiments have a limited value and until now they have consisted largely, in the field of endocrinology, of the ablation and feeding experiments. Such experiments have their inherent limitations. It must also be remembered that experimental efforts to solve clinical problems are valuable if they produce positive findings that can be corroborated. Negative

results of animal experimentation can not be crucial. They merely establish some degree of antecedent doubt as to what may be found clinically if the conditions of the experiment are similar to those of the clinical state.

The positive achievements which I have attempted to outline certainly indicate that endocrinology has a definite place in medicine, and that it has contributed more than its proportionate share to the advancement of clinical medicine and therapy. It has shortcomings, which are no more than the shortcomings of medicine in general today. It is a branch of medicine that is worthy of the serious investigation of the best clinicians and the best laboratory workers. But progress can most rapidly be made when both clinician and laboratory worker have only one object: the search for truth. Both must appreciate the positive contributions as well as the negative and questionable data of the other.

Book Reviews

DISEASES OF THE THYROID GLAND. Arthur E. Hertzler; with chapter on hospital management by Victor E. Chesky. St. Louis, 1922. C. V. Mosby Co. 245 p. 8°.

Unlike many monographs, this book comprises very largely the personal experience of the author. This lends it unique value as well as leads to some conclusions that many surgeons will dispute. The study is based on many years of work with a somewhat localized group of patients, and opportunities for effective follow-up work have been unusual. Possibly for this reason the author is by no means enthusiastic as to the ultimate results of thyroid extirpation. "The best that can be said of the operative treatment," he writes, "is that it is the best we have to offer the patient. . . . Fewer patients succumb from the operation than from the disease untouched."

He does not believe in the existence of "innocent goitres" but that, although they may exist for ten to forty years, they usually ultimately kill by undergoing toxic or malignant degeneration. "Personally, I categorically refuse," he says, "to treat colloid goitre—other than by operation."

The author is particularly to be commended in that he eschews the dubious term "hyperthyroidism" for the various sorts of thyroid intoxication. His use of words, in some other instances, however, is unfortunate. The constant use of "she" as generic for goitre patient is more or less of a libel. He also says he "operates" his patients—a fact which his reputation renders very doubtful. He even operates "cases." Such shop jargon has no place in a book so carefully written. The interpolation of bibliographic references immediately in the text is distracting.

Another unfortunate feature in the work is the publication of numerous mediocre photographs by way of illustrations. This practice, which is by no means uncommon, seems to be adopted on the supposition that the subjective element is thereby eliminated, it being forgotten that in the selection of specimens to photograph a high degree of subjectivity is inevitable. A comparison of the excellent drawings in the latter part of the book with the reproduced photographs brings out strikingly the inferiority of the latter.

The use of a high gloss, thick paper is annoying both to the retina and to the fiduciary consciousness of the reader.

So much for adverse comments. They are of minor importance when compared with the many excellent features. The book as a whole is readable, and in some places, delightful for its racy diction. It is one which can be highly recommended, both as a repository of the wisdom of an experienced and careful student of goitre and as one the reading of which is a pleasure rather than a task. To the surgeon, of the technical aspects of the book, the graphic presentation of the art of thyroidectomy under local anesthesia will perhaps most appeal.—R. G. H.

A PSYCHOANALYTIC STUDY OF PSYCHOSES WITH ENDOCRINOSES. Dudley Ward Fay. Washington, 1922. Nervous and Mental Disease Publishing Company. 122 p. 8°.

The author reports a study of the case histories of 22 male patients afflicted with psychoses, either pure schizopherenia or other psychoses with schizopherenic features. These were selected cases with endocrine involvement, mostly "submyxedema." The book is taken up very largely with Freudian psychopathology. Not enough endocrine data are included to permit a satisfactory judgment as to the presence or absence of endocrine features. The endocrine material administered was, for the most part, desiccated thyroid gland. In one or two instances, this seemed to increase the troubles, but as a rule the effect appeared to be beneficial in varying degrees. One gets the impression that the actual effect was to increase the available energy of the patients and to give them a feeling of being more competent to cope with their environment. The beneficial effects appeared to be temporary, although in one instance the immediate benefit was spectacular.

In view of the paucity of endocrine data, the study cannot be regarded as of very great value as tangible evidence. It does indicate that the problem as studied is worthy of much more extensive investigation. The author feels that a combination of thyroid stimulation and psychoanalysis may prove an excellent method of attacking incipient schizopherenia.—R. G. H.

EXOPHTHALMIC GOITER. Walter Edmunds, London, 1922, 2d ed. Ballière, Tindall & Cox. 36 p.

This little book embodies a lecture delivered at a London postgraduate college in 1921. It may be recommended to general practitioners who care to read a brief account of modern views on Graves' disease. Edmunds states that the secretory nerves of

the thyroid arise from the middle cervical ganglion. However, in most cases man has no middle cervical ganglion, but only a ganglion supremum and stellatum.—J. K.

LE GOITRE ENDEMIQUE. Dr. F. Messerli, Lausanne, 1916. Editeur, E. Frankfurter. 179 p.

The author concludes that no relation exists between goiter and the geological constitution of the country. He attributes goiter to an infection of the water with a specific micro-organism and even describes a culture-medium to cultivate the virus. Goiter is caused not only by the drinking water, but also by contact, by the stools, by the sputa, etc. Modern experiments have not yet sustained this theory.—J. K.

DIE LEHRE VON DER INNEREN SEKRETION. E. Gley. Bern & Leipzig, 1920.

A translation of Prof. Gley's well known monograph into German, by Dr. A. Lipschütz. For review, see Monatschr. f. Kinderh. (Leipz.), 1922, **22**, 715.—R. G. H.

DIE MASTURBATION. Hermann Rohleder. Berl., 1921. 384 p.

Among other topics the author discusses endocrine relationships. For review, see Monatschr. f. Kinderh. (Leipz.), 1922, **22**, 720.—R. G. H.

BASAL METABOLISM: ITS DETERMINATION AND APPLICATION. Edited by Frank B. Sanborn, Boston. Sanborn Co. 282 p.

A series of reprints of original articles by authorities on various aspects of basal metabolism.—R. G. H.

SENESCENCE. THE LAST HALF OF LIFE. G. Stanley Hall., Ph.D., LL.D. D. Appleton & Company, N. Y., 1922. 518 p.

This book is an admirable presentation of the *raison d'etre* of old age. In it is given the youth of old age, or the climacteric, the history of old age, literature by and on old age, statistics of old age and its care, medical views and treatment of old age, the contributions of biology and physiology to the understanding of old age, the answers to a questionnaire sent out by the author to oldsters, the conclusions drawn from the observations of the author and an excellent chapter on the psychology of death.

The part played by the incretions in the changes incident to the onset of the last half of life and their participation in the ultimate disintegration are rather sketchily given. Hall leans toward the Freudian psychology to the extent that he states, "I think I would gladly offer myself as a *corpus vile* for the Steinach operation to study its psychological effects at first hand." His philosophy of death is eminently materialistic.—F. S. H.

Abstract Department

A function of the ADRENAL cortex (Ueber eine Funktion der Nebennierenrinde). Adler (L.), München. med. Wchnschr., 1922, **69**, 797; Klin. Wchnschr. (Berl.), 1922, **1**, 1281.

A dried adenoma of adrenal was given to tadpoles. The animals showed a tremendous growth and only male animals (at least when frogs were used) developed.—J. K.

Correlation of ADRENAL weight with fetal development (Gli indici ponderali dei surreni in funzione della lunghezza e del peso del prodotto di concepimento). Cazzaniga (A.), Sperimentale. Arch. di biol. (Firenze), 1922, **76**, 121-129.

The author has studied the growth curve of the human adrenal before birth, considering biometrically the absolute weights and the correlation weight index with the stature and the body weight together with the average deviation. He found that in the last month of pregnancy there is a retardation of increase in the fetal length and weight, and at the same time a marked augmentation of the suprarenal weight. During this period the growth of the body is not under the direct influence of these glands. At this time the nerve fibres undergo marked development and lipoid grains appear in the pulmonary alveoli. It would seem probable that this latter phenomenon and the myelinization of the nerve fibres are correlated with lipoid metabolism in the adrenals.—P. M. N.

An indistinct or atypical form of so-called ADRENAL VIRILISM (Formes frustes du virilisme dit surrénal). Claude (H.), Encéphale (Paris), 1921, **16**, 491-495.

The author has observed a large number of cases of virilism which he designates "formes frustes" because the physical and psycho-sexual disturbances are little in evidence and because the glandular (endocrine) dysfunction is in general not apparent. It appears that in this type of virilism the dystrophia may be brought about in the absence of tumors of the suprarenals by lutein hyperplasia in the ovaries with secondary reaction on the suprarenals. Since lutein cells as well as the cells of the suprarenal cortex are derived from the wolffian body, he suggests that wolffian virilism might be used instead of suprarenal virilism. One case is given in detail. In this patient sexual precocity began at the age of 7. At the time of puberty (at age of 11) a physical and moral change

occurred. She became timid and reserved. At the age of 18 a growth of hair appeared on her face and in other ways she began to change towards the masculine type. When examined at the age of 37 she was melancholiac. The mental disturbances were apparently secondary to the organic. There was sexual frigidity and very irregular menstruation. Biological tests indicated insufficiency of the **thyroid** and slightly of the suprarenals. Under treatment she improved. No literature given.—A. T. R.

The action of ADRENIN on the leucocytes and erythrocytes. Cowie (D. M.), Contrib. Med. & Biol. Research (Osler), 1919, **2**, 829-844.

Cowie reports that the injection of adrenalin causes an initial rise in the leucocytes followed by a decline within one hour. At the second hour a further rise occurs and may last eight hours. All varieties of leucocytes participate. The red cells show similar rises. In both cases these are interpreted as being purely mechanical in origin.—Med. Sc., 1921, **3**, 392.

Observations on the functional activity of the SUPRARENALS in health and disease. Cramer (W.), Scient. Rep. Imp. Cancer Research Fund (Lond.), 1919, **6**, 1-21.

Experiments mostly on mice, rats and rabbits show that the suprarenal gland and in particular the medulla is profoundly affected in a number of conditions (exposure to cold, fever and bacterial infections) associated with disturbances in the heat regulating mechanism. Changes in the functional activity of the medulla of the suprarenals, as evidenced by histological demonstration of **adrenalin** granules, were also observed in experimental **hyperthyroidism**, experimental acidosis, severe hemorrhage, anaesthesia and post-operative shock. In some cases there were also changes in the medulla of the suprarenals and in the thyroid gland. These observations are considered to be further evidence in support of the idea that the thyroid and suprarenals form a heat regulating apparatus which supplements the nervous mechanism. How this apparatus probably operates is discussed. The practical bearing of these points on specific treatment of certain conditions is brought out. The article is well illustrated. Twenty-one references are given.

—A. T. R.

On the simultaneous effects of ADRENALINE and papaverine in the human organism (Hungarian). Csépai (K.), Orvosi hetil. (Budapest), 1921, **65**, 153-160.

The antagonistic effects of adrenaline and papaverine on the blood pressure in dogs are confirmed. In man, however, papaverine enhances the pressor effect of adrenaline. The use of papaverine instead of pituitrin, in combination with adrenaline, is recommended for therapeutic purposes.—Physiol. Abst., **7**, 133.

ADRENAL ablation in epilepsy (Nebennierenentfernung bei Epilepsie). Engelbrecht (v.), Klin. Wchnschr. (Berl.), 1922, **1**, 1282.

A short note. Operation did not improve the epilepsy.—J. K.

Habitual vomiting and ptyalism of pregnancy treated with ADRENIN (Vomissements tenaces de la gestation, ptyalisme traités par l'adrénaline). Favreau, Soc. de méd. et de chir. de Bordeaux, 1922; abst., J. de méd. de Bordeaux, 1922, **94**, 430.

Favreau reports the case of a woman of 27 who had been habitually constipated since her second pregnancy and who was troubled with frequent vomiting. Her general condition was precarious; the urine was scanty, turbid and bile-colored. There was also continuous ptyalism. Since cold drinks did not help the constipation adrenin was prescribed. Five days later the vomiting was diminished and 8 days after the beginning of the treatment there was neither vomiting nor salivation.—R. G. H.

Influence of ADRENIN in man (Über die Gefässwirkung des Adrenalins beim Menschen). Fornet (B.), Arch. f. exper. Path. u. Pharmacol. (Leipz.), 1922, **92**, 165-172.

The statement of Straub and Ritzmann, that of adrenaline injected subcutaneously only 6% reaches the blood stream, is not true for human subjects. If adrenaline is injected intravenously into the forearm after a ligature has been previously applied to the arm so that the pulse is obliterated distal to the ligature, and if 10 minutes after the intravenous injection the ligature is removed, the typical adrenaline action takes place. The author considers that this proves that adrenaline is not destroyed in the blood stream. Neither is adrenaline destroyed in the subcutaneous tissues.

—Physiol. Abst., **7**, 258.

The antagonistic action of caffein and ADRENIN on the isolated intestine (Action antagoniste de la caféine et de l'adrénaline sur l'intestin isolé). Fredericq (H.) & Mélon (L.), Compt. rend. Soc. de biol. (Par.), 1922, **87**, 92-94.

The action of caffein on the isolated rabbit intestine is antagonistic to that of adrenalin. Caffein causes the tonus and contractions which have been abolished by adrenalin to reappear. Adrenalin, on the other hand, reduces the augmented tonus produced by a previous treatment with caffein. Caffein, therefore, acts as an antagonist to the sympathico-mimetic action of adrenalin.—W. B. C.

Influence of ADRENAL, HYPOPHYSIS and PINEAL feeding on cutaneous pigmentation and respiratory rhythm of Salmo fario (Influenza dell' alimentazione con capsule surrenali, ipofisi ed epifisi su la pigmentazione cutanea, ed il ritmo respiratorio di "Salmo fario"). Gianferrari (Luisa), Arch. di sc. biol. (Napoli), 1922, **3**, 39-52.

The author has studied the young fry of Salmo fario, because the action of nerves on the pigmentation is well known, because these fish are subject to rapid variations of cutaneous color, and it is easier to determine the modifications of increase of blood in the gills, in relation to the modification of the respiratory rhythm. Whether the fry are fasted or fed with plankton or with spleen the results are the same. Animals in five receptacles were fed respectively adrenal medullary substance, adrenal cortex, adrenal whole gland, hypophysis and pineal of the horse. Only a few ate the medullary substance. Those that did so lost the color of their skin in four or five hours, remaining yellowish-white for two days; on the fourth day they were almost all repigmented. Those that refused to eat the substance retained their normal color. The depigmentation began with a band behind the gills, and thence extended over the whole body. The author concluded that the phenomenon depended on the material ingested and not on glandular substances dissolved in the water which acted externally, since some were put into a receptacle with clean water as soon as they had eaten and lost their color the same as the others. Together with this depigmentation they presented dyspnoea; the gills appeared turgid, hyperemic and with larger spaces between the gill arches; they remained stationary at the bottom of the receptacle. When the color came back all the other symptoms disappeared. If, after having recovered their normal state, they again ate adrenal substance, they were subjected to the same modifications, but before recovering their normal color they died. Eating cortical substance alone did not cause any alteration except in case of a few animals that probably obtained a small amount of medullary substance with the cortical preparation. Hypophysis feeding caused depigmentation of less intensity but longer duration than did adrenal feeding. Pineal feeding gave a similar effect, but it did not produce any action on respiration. These experiments indicate that contraction of the chromatophore cells is determined by the sympathic system, since adrenalin acts selectively on this system and hypophysis and perhaps the pineal have some connection with it.—P. M. N.

The action of ADRENIN on the blood picture in leukemias (L'action de l'adrénaline sur le tableau leucocytaire dans les myéloses). Goia (J.), Presse méd. (Par.), 1922, **30**, 366-369.

Goia studied the effect of injections of adrenalin in pathologic conditions of the blood on two cases of myelogenous leukemia, two cases of (lymphocytic) pseudoleukemia and in one splenectomized patient. He used 0.001 (cc?) of "Tonogen" Richter, subcutaneously. Blood counts were made 10', 20, 30 and 60 minutes as well as 3 and 6 hours after injection. He found that in myologenous leukemias the total leucocyte count rose from 380,000 to 460,000 at the end of 10 minutes and to 580,000 at the end of 20 minutes, by a rapid in-

crease of myelocytes and myeloblasts; the lymphocytes showed a slight increase at first, but later a marked reduction in numbers. In pseudoleukemias the leucocytic reaction was the result of a rapid increase of the lymphocytes. In chronic myologenous leukemias in which very few myelocytes and myeloblasts were found in the blood before injection, the leucocytosis was again predominantly myelocytic. After splenectomy the leucocytosis was also marked, but the lymphocytes as well as the myelocytes and the polymorph neutrophils increased. Goia concludes that the reaction to adrenalin shows a stimulation of tissues capable of response, either lymph nodes and spleen or bone marrow. The hypertrophy of the marrow with retrogression of the lymph glands explains the myelocytic reaction in myologenous leukemia, the intact condition of the lymphoid elements in pseudoleukemia the predominance of the lymphocytis reaction in the latter. He suggests that injections of adrenalin may be of value to establish the differential diagnosis, which is often difficult in cases of chronic myologenous leukemia and pseudoleukemia.

—G. L.

The mechanism of hyperglycemia after the injection of ADRENIN (Untersuchungen über den Mechanismus der Adrenalinhyperglycaemie). Gottschalk (A.) & Pohle (E.), Klin. Wchnschr. (Berl.), 1922, **1**, 1310-1311.

Continuous intravenous infusion of a diluted solution of adrenalin or subcutaneous injection of enough to produce hyperglycemia produces a very marked rise of the hydrogen ions and concentration of the blood in the vena porta and vena hepatica. This rise reaches its maximum in the capillaries of the vena porta. If a quantity of alkali is first administered, hyperglycemia is much less marked. Therefore, the authors conclude that increased acidity of the blood is a "conditio sine qua non" for adrenin hyperglycemia.

—J. K.

Epithelial tumor of the ADRENAL (Epithelialer Tumor der Nebenniere). Horner, Deutsche med. Wchnschr. (Berl.), 1922, **48**, 886.

No details are given.—J. K.

(ADRENIN) Hyperglycemia in diseases with hypertonia (Zur Frage der Hyperglykämie bei Krankheitszuständen mit Hochdruck). Kahler (H.), Wien. Arch. f. innere Med., 1922, **4**, 129-148.

Kahler could not confirm the view of many investigators that there is hyperglycemia in all cases of hypertonia. Many patients with high blood pressure have a perfectly normal quantity of blood sugar. Hyperglycemia, however, is very often found when there are complications, as in apoplexy, eclampsia or uremia; it is also found in "essential hypertonia" with sclerosis of the vessels of the pancreas and in cases with stasis of the blood. When adrenalin is injected in patients with a high blood pressure, the effect is just the

same as in normal persons. This fact and the fact that in a large number of patients with hypertonia there is no hyperglycemia make it improbable that hyperadrenalinemia is the cause of hypertonia. When a high blood pressure is complicated by stasis of the blood there is always hyperglycemia. It is possible, but not probable, that this is caused by hyperadrenalinemia.—J. K.

Histochemistry of melanin and ADRENIN (Histochemie des Melanins und des Adrenalins). Kutschera (H.), Wien. klin. Wchnschr., 1922, **35**, 554.

Ammoniacal silver nitrate may be reduced in vitrio by catechol and in the tissues by melanin and adrenalin. In the **liver**, heart and **adrenals** a pigment (lipofuchsin) is found which, after its fats are extracted, also reduces ammoniacal silver nitrate. Lipofuchsin is probably melanin, surrounded by lipoids. Adrenalin finds its origin in the protoplasm of the cells of the medulla of the adrenals, sometimes transported into the cortex. The capillaries of the cortex have communications with the veins of the pancreas. The chromaffin substance is very sensitive to some substances. It is destroyed by prussic acid, by heat and by cold. From this we may conclude that the chromaffin substance has some properties in common with the enzymes. As this is not the case with adrenalin, the chromaffin substance is not identical with adrenalin, but may play a certain rôle in its formation.—J. K.

Blood pressure after the injection of ADRENIN in hypertonia (Adrenalinblutdrucksreaktion bei Hypertonisten). Kylin (E.), Zentralbl. f. innere Med. (Leipz.), 1922, **43**, 329-331.

Some time ago Kylin pointed out that the blood pressure is often high in **diabetes**, especially in elderly persons. He therefore believed that there might be a certain relation between the endocrine disturbances in hypertonia and in senile diabetes. He injected 1 mg. of adrenalin subcutaneously in healthy persons and in patients. The blood pressure curve in acute nephritis is the same as that in healthy persons. In 14 cases of hypertonia from benign sclerosis of the kidney 13 patients showed an abnormal reaction. During the first 15-20 minutes after the injection the blood pressure may sink 40-50 mm., rising again to its original height or even higher. This abnormal reaction makes it highly probable that endocrine disturbances have some relation to the pathogenesis of benign sclerosis of the kidney and to hypertonia.—J. K.

Gastric crises and paroxysmal hypertension related to an ADRENAL tumor (Crises solaires et hypertension paroxystique en rapport avec une tumeur surrénale). Labbé (M.), Tinel (J.) & Doumer, Bull. et mém. Soc. méd. des hôp. de Par., 1922, **46**, 982-990.

A characteristic detailed case report of paroxysmal neural crises, of epigastric constriction, nausea, vomiting and vaso-motor disturb-

ances accompanied by arterial hypertension and terminating fatally. At autopsy the left adrenal was found to have been replaced by a tumor the size of a large mandarin orange, and having the medullary structure of the adrenal. The other endocrine glands seemed normal in size. The thyroid section showed evidence of heightened activity. The relation between this probable hyperepinephrinemia and the antermotrem symptoms is stressed.—F. S. H.

Malign neuroblastoma of the sympathetic in the right ADRENAL (Ein malignes Neuroblastom des Sympathicus in der rechten Nebenniere). Lauche, Klin. Wchnschr. (Berl.), 1922, **1**, 1233.

No details are given except that a girl of 3½ months had a tumor with metastasis in the liver.—J. K.

(ADRENAL) Thomsen's disease of amyotrophic type (Maladie de Thomsen fruste à type amyotrophique). Lecaplain & Billard, Normandie méd. (Rouen), 1922, **33**, No. 3; abst., Presse méd. (Par.), 1922, **30**, 492.

A case is described of Thomsen's disease of amyotrophic type. The syndrome is progressive, bearing always upon the extremity of the superior members and accompanied by slight signs of adrenal insufficiency. There are also signs of degeneracy, but with familial character. This case is comparable to an observation recently published by Roger and Aymès.—R. G. H.

The influence of ADRENIN on the ocular pressure and on the blood pressure, general and retinal (De l'influence de l'adrenaline sur la tension oculaire et sur la tension sanguine générale et rétinienne chez l'homme). Leplat (G.), Ann. d'ocul., 1921, **158**, 414-423.

Injection of adrenaline produces a rise of pressure in the central retinal artery parallel to that produced in the general arterial system; rise of intra-ocular pressure was not observed. Instillation of adrenaline leads to a slight fall of intra-ocular pressure with no change of retinal arterial pressure. Changes of intra-ocular pressure are independent of changes of retinal venous pressure.

—Physiol. Abst., **7**, 259.

Is ADRENIN a hormone (È l'adrenalina un ormone)? Marfori (P.), Arch. intern. de pharmacod. et de thérap. (Brux.), 1921, **26**, 137-149.

A critical and experimental publication directed to the examination and the interpretation of Gley's experiments, denying not only the harmonic character of adrenalin but also every other normal function in the organism. Marfori has demonstrated that if from an animal with high blood pressure—caused by injection of the minimum of adrenalin sufficient to produce some effect—we

take 30 or 40 cc. to reinject in the same animal after it has become normal or in another animal in good health, there is no modification in blood pressure. A minimum of adrenalin in the blood is necessary to manifest its action. It is probable that in Gley and Quinquaud's experiments the adrenin was insufficient to produce definitely increased blood pressure. The problem as to the hormonic nature of the endocrinal products cannot be solved with only physiological or pharmacological experimentation, but anatomical, pathological and clinical data must also be considered.—G. C.

Partial ADRENAL deficiency (Ueber einseitigen Nebennierenmangel). Miloslavich (E.), Zentralbl. f. allg. Path. u. path. Anat. (Jena), 1920, **30**, 465-470.

Developmental disturbances of the adrenals have been observed chiefly in non-viable infants and are usually associated with serious defects of the central nervous system. Miloslavich has collected 8 cases of absence of one adrenal in children and adults and adds one case of his own. His patient was a 72-year-old female dwarf. There was complete absence of the right kidney, right adrenal and no trace of the renal and adrenal arteries on the right side could be found. There were, further, malformations of the intestine and polydactylism of both hands and feet. In all of the cases collected from the literature it was the right adrenal that was absent.—J. P. S.

Effects of ADRENALECTOMY on the automatic contractions of the isolated duodenum of the rabbit (Effets de la l'ablation des surrénales sur les contractions automatiques du duodénum isolé du lapin). de Mira (F.) & Fontes (G.), J. de physiol. et de path. gén. (Par.), 1921, **19**, 1-12.

The spontaneous contractions of the excised duodenum of rabbits, from which the adrenals have been removed, are very small or absent. The effect is present even in an hour. Controls show that it is neither due to anesthetic nor to shock. The inhibitory reaction to adrenalin is apparently unaffected. Adrenalin itself was unable to supply the deficiency of the whole adrenal. The injection of adrenal extract after the removal of the adrenals, prevents the appearance of inactivity in the duodenum fifteen minutes after the injection. It is suggested that the cortex is responsible.

—Physiol. Abst.

Surgery of the ADRENALS (Grundsätzliche Fragen in der Chirurgie der Nebennieren). Peiper (H.), Klin. Wchnschr. (Berl.), 1922, **1**, 161-163.

Removal of an adrenal has been recommended by Stephan in polycythemia and by Fischer and Brunings in epilepsy. There have been no definite results in this operation in polycythemia up to this time. The great difficulty in the surgery of the adrenal is com-

pensatory hypertrophy, but this is not constant. One adrenal was removed in a very severe case of epilepsy, but operation had no effect. Ten months later the patient died of typhus. At the post-mortem examination no trace of hypertrophy of the other adrenal was found.—J. K.

The lipoid content of the ADRENAL cortex of the guinea pig in experimental scurvy (Über den Lipoid-gehalt der Nebennierenrinde des Meerschweinchens bei experimentellem Skorbut). Peiper (H.), Klin. Wchnschr. (Berl.), 1922, **1**, 1263-1264.

When guinea pigs die from starvation or cachexia the cortex of the adrenals contains large amounts of lipoids. When they die from experimental scurvy, little or no lipoids are found. If vitamine C is given to animals with scurvy the adrenals (first the outer layers of the zona fasciculata) become very rich in lipoids.—J. K.

(ADRENIN) Action of blood, plasma, red cells, normal and asphyxiated, on the isolated intestine (Action du sang, du plasma, des globules rouges normaux et asphyxiés sur l'intestin isolé). Pellegrini (R.), Arch. internat. de physiol. (Liége & Par.), 1921, **17**, 209-226.

The author does not admit the existence of adrenalin in normal circulating blood, but frequently finds in whole hirudin-treated or fibrinated blood, in the plasma, in the red cells and in the serum, substances having a tonic action on the intestine. These substances are thermolabile. Asphyxia increases them. Physiol. Abst., **6**, 582.

(ADRENIN) Influence of light rays on carbohydrate metabolism (Über die Beeinflussung des Stoffwechsels der Kohlehydrate durch Strahlung). Pincussen (L.), Klin. Wchnschr. (Berl.), 1922, **1**, 174.

When a rabbit is exposed to light rays and adrenalin is injected the blood sugar is much higher than after a simple injection. Light rays after injection of eosin decrease the blood sugar. When the rabbit gets eosin first, is exposed afterwards to light rays, and then gets adrenalin, the blood sugar is raised, but not so much as it is in the animals which did not receive eosin. In diabetes it is often possible to diminish the blood sugar markedly after injection of eosin; even the acetone bodies sometimes disappear from the urine. In hypophyseal diabetes (with polyuria) light rays have no effect. —J. K.

The action of atropin, ADRENIN, and pilocarpin (Zur Wirkung des Atropins, Adrenalins und Pilokarpins). Platz, München. med. Wchnschr., 1922, **69**, 727.

Atropin was given in doses of 0.05 to 1 mg. When the dose is less than 0.5 mg. the pulse becomes slower. When larger doses are

given intravenously the pulse rate at once increases; when given subcutaneously there is first bradycardia, followed by tachycardia. Adrenalin was injected into 121 patients. Even 0.001 mg. given intravenously produces a marked rise of blood pressure. The increase of the blood pressure does not parallel the quantity of adrenalin injected. In 116 of the 121 patients adrenalin caused an increased pulse rate. After intravenous injection respiration is quickened and the blood sugar and NaCl in the blood is increased. Erythrocytes and leucocytes are increased along with neutropenia, eosinphilia, and lymphocytosis. The mononuclears may be increased or decreased. General symptoms, such as headache, giddiness and paleness are much more marked after intravenous than after subcutaneous injections. Even 18 mg. of adrenalin given intrarectal have no effect. Pilocarpin always increases the pulse rate and causes the blood pressure to sink and the blood sugar to increase.—J. K.

The influence of pilocarpin, ADRENIN and atropin in the study of the involuntary nervous system (Die Wirkung des Pilocarpins, Adrenalins und Atropins als Beitrag zur Prufung des vegetativen Nervensystems). Platz (O.), Klin. Wchnschr. (Berl.), 1922, **1**, 1230; Deutsche med. Wchnschr. (Berl.), 1922, **48**, 788.

Pilocarpin, adrenalin or atropin may have quite different effects according to whether they are injected subcutaneously or intravenously. For the pharmacological study of the irritability of the vegetative nervous system, it is best to inject them directly into the veins. However, their action is often too severe if this method is used.—J. K.

Lesions of the vessel-walls caused by ADRENIN (Sulle alterazioni delle pareti vascolari prodotte dall' adrenalina sia per iniezione in circolo, sia per contatto). Polettini (B.), Arch. per le sc. med. (Torino), 1920, **43**, 63-92.

Repeated intravenous or intraperitoneal injections of fractional doses of adrenalin, constantly cause, in rabbits, aortic changes consisting of degeneration and necrosis of the plain muscle-fibres of the middle coat. These lesions are followed by distension, atrophy, fragmentation, and destruction of the elastic fibres. The degenerated places in the aorta become lastly extensively calcified. These alterations are identical with those found in the aortae of rabbits, the subjects of idiopathic arteriosclerosis; hence the conclusion that the arteriosclerosis of rabbits can be experimentally reproduced. If adrenalin is directly applied to the walls of arteries, such as the carotid or the femoral, lesions can be observed which do not essentially differ from those caused by injections of adrenalin. But if adrenalin is directly injected into the urinary bladder no lesions of the plain muscle-fibres are produced, but only haemorrhages per diapedes from the blood-vessels of the submucosa. These facts sug-

gest the conclusion that the arteriosclerotic changes caused by adrenalin are very likely due to a local and direct influence exercised on the muscle-fibres of the arterial walls and only in part or very little to the hypertension which follows the passage of adrenalin into the blood-stream. How it is that the influence of adrenalin is felt by the muscle-fibres of blood-vessels and not by those of the wall of the bladder remains as obscure as the selective action of certain drugs and other substances on determined cells or tissues.

—Med. Sc., 1921, **3**, 372.

(ADRENIN) The treatment of uncontrollable vomiting (Discussion sur le traitement des vomissements incoercibles). Rathery, Soc. d'obst. et de gynéc., 1922 (May 8); abst., Presse méd. (Par.), 1922, **30**, 480-481.

Rathery describes the therapeutic results which he obtained in pregnant women (primaparae and multiparae) who, from the second month, had been in a serious condition due to incessant vomiting. Asthenia, very marked, was accompanied by a low temperature, by arterial tension of about 100/60 to 90/50 and by a very rapid pulse. The urine, which was much diminished, revealed the presence of acetone. Radioscopy showed gastric myasthenia. Adrenin was given in doses of 1-2 mg. a day for 1-7 days. The author emphasizes the rapid action of the drug; vomiting ceases quickly, asthenia diminishes, the pulse rate is lowered, and the urinary acidosis disappears. If the adrenin administration is stopped Gerhardt reaction appears again in the urine. There is a very obivous relation between adrenin and acidosis. The action of adrenin is lasting—the author has never seen vomiting reappear. Rathery believes these good results are due to the action of the proper medicament rather than to a possible pluriglandular insufficiency.—R. G. H.

Some technical points in the method of physiological control of ADRENALIN products. Richaud (A.), J. de pharm. et chim. (Par.), 1922, **25**, 289-298.

The necessity of washing the adrenalin from the cannula after each injection by Cushny's control method is discussed. From the tracings obtained upon injecting, for comparison, solutions of unknown and known strengths of adrenalin, Richaud deduces the increase of blood pressure (which is a function of the adrenalin contents), by drawing the heights of the curves. A graph made from these increments as ordinates and the concentrations of the solutions used as abscissas, gives a direct means of comparison.

—Chem. Abst., **16**, 2385.

Blood sugar in Addison's disease and the influence of ADRENIN (Der Blutzucker bei Addisonscher Krankheit and seine Beeinflussung durch Adrenalin). Rosenow (G.), & Jaguttis, Klin. Wchnschr. (Berl.), 1922, **1**, 358-360.

Most authors describe hypoglycemia as a classical symptom of Addison's disease, but in Addison's disease, just as in normal persons, the blood sugar varies decidedly, and it may happen that a patient may show hypoglycemia one morning and normal quantity of blood sugar the next day. For the diagnosis of "hypoglycemic Addison" it is necessary to determine the blood sugar for a number of consecutive days on an empty stomach. When adrenalin is injected into a patient with Addison's disease, the blood sugar rises, but to a much less extent than would be the case in normal persons. The maximum, just as in normal persons, is reached in ± 1 hour. Normal persons often show a secondary hypoglycemia after "adrenalin-hyperglycemia." This hypoglycemia was not found in Addison's disease.—J. K.

Hemoclasic agonal tabetic crises treated with ADRENIN (Crises algiciques tabétiques hemoclasiques. Leur traitment par l'adrénaline). Sicard & Lermoyez (J.), Bull. et mém. Soc. méd. des hôp. de Par., 1922, **46**, 797-801.

The slow intravenous injection of 0.5 mg. of adrenin in 10 cc. of artificial serum into 3 tabetic patients gave relief when no other medication was effective. Improvement occurred in from one-half to two hours. The dose can be repeated after several hours.

—F. S. H.

Unilateral ADRENAL ablation in man (Die Einseitige Entfernung der Nebenniere beim Menschen). Steinthal, Klin. Wchnschr. (Berl.), 1922, **1**, 1258-1260.

Effect from operation in epilepsy was seen only in an infantile boy of 15, who had no attacks for over a year after the ablation of an adrenal. Why this boy was cured, or at least markedly improved is unknown. It has been repeatedly stated that ablation of one adrenal always gives rise to hypertrophy of the second, but this is not at all certain. Peiper has described a case in which at autopsy 10 months after the ablation of one adrenal there was no trace of hypertrophy of the second. Steinthal also reports a case in which the operation brought no good results and the patient died 10 months after the operation. At autopsy it was seen that the remaining adrenal weighed 10.5 gm. whereas the adrenal that had been removed weighed 3 gm. (Simmonds, however, considers 10 gm. to be a normal weight.) In the **hypophysis** a small zona intermedia and an under-developed pars nervosa were found; the **thyroid** showed a colloid **goiter**, the **ovaries** and the **thymus** showed nothing of especial interest.—J. K.

Are the practical effects of extirpation in hyperfunction of the ADRENALS local or in higher nervous centers (Welche praktischen Erfolge seitigt die Exstirpation bei Hyperfunktion der

Nebenniere selbst oder von deren zentral übergeordieten Zentren)? Stephan & Floercken, Klin. Wchnschr. (Berl.), 1922, **1**, 1128.

In two cases of hypertonia ablation of an adrenal had no effect (only the number of erythrocytes was diminished). X-ray treatment of the adrenals causes atrophy of the cortex and has no influence on the chromaffin tissue.—J. K.

Injection of ADRENIN in lunatics (Adrenalin proef inspuitingen bij geestesszieken). Stuurman (F. J.), Nederl. Maandschr. v. Geneesk. (Leiden), 1922, **3**, 44-60.

Subcutaneous injection of 0.7 mg. of adrenalin causes an increased systolic blood pressure and an increased pulse rate. The diastolic pressure generally sinks or remains unaltered; in very rare cases it is increased also. Persons suffering with schizophrenia show a less marked reaction than other lunatics. The paranoiac form shows a more intense reaction than the catatonic or the hebephrenic forms. Epileptic patients show a diminished reaction of pulse and blood pressure; they often develop glucosuria. Maniac-depressive patients show a rather intense reaction, especially the unquiet forms of melancholia, who generally have a high blood pressure. Administration of alkali diminishes the effect of adrenalin. It is probable that in melancholia adrenalin increases the anxiety. It is important, therefore, to try out the effect of alkali in this disease.—J. K.

Extirpation of the ADRENALS in epilepsy (Über Nebennierenexstirpation bei Epilepsie). Sultan, Klin. Wchnschr. (Berl.), 1922, **1**, 145.

See Endocrin., 1922, **6**, 535.—J. K.

(ADRENAL) Ethmoid-orbital metastasis of latent hypernephroma (Métastase ethmoïde orbitaire d'un hypernéphrome latent). Van Duyse & Marbaix, Brux. Méd., 1922, **2**, 423-425.

A tumor was removed from the ethmoid showing the histological picture of hypernephroma. Though no clinical symptoms of a primary tumor were present, on the roentgenogram a large shadow was seen between the left kidney and the vertebral column, caused perhaps by a primary tumor.—J. K.

Histological changes in the ADRENALS during pregnancy (Comment faut-il comprendre, au point de vue histologique, le fonctionnement des capsules surrénales au cours de la gestation 1re note)? Watrin (J.), Rev. méd. de l'est (Nancy), 1920, **48**, 349-353.

Thirty-two out of 35 rabbits showed hypertrophy and evidences of hypersecretion in the cortical zone (medulla apparently not involved) which was already visible on the fifth day following fecundation. By the thirtieth day of pregnancy the suprarenal averaged more

than double, and was occasionally three times its normal size. Most of the increase was in the zona fasciculata due to an increase in the size of the cells and to encroachment upon neighboring zones. There was but little evidence of cell division.—A. T. R.

(ADRENAL) A case of tumor of the fourth ventricle of the brain, accompanied by cutaneous pigmentation like that of Addison's disease. Weber (F. P.), Internat. Clin. (Phila.), 1922, **2**, 93-101.

A girl of 14 was suffering with nervous restlessness, excitement, vomiting, rapid pulse, and irregular fever. She was emaciated, and there was considerable cutaneous pigmentation resembling that of Addison's disease. Laboratory reports were negative. Seventeen days after admission to the hospital the patient became stuporous, and death occurred 12 days thereafter. The pigmentation of the trunk had apparently increased while in the hospital. Autopsy revealed a tumor about the size of a large acorn, growing within the fourth ventricle of the brain. No evidence of disease of the suprarenal glands was discovered. The author suggests that the cutaneous pigmentation "may have been in some unknown way a result of the gliomatous disease of the brain."—I. B.

Influence of ADRENIN in different concentrations on blood pressure and blood sugar (Adrenalinwirkung auf Blutdruck und Blutzucker bei verschiedener Konzentration). Weinberg, München. med. Wchnschr., 1922, **69**, 797; Klin. Wchnschr. (Berl.), 1922, **1**, 1282.

Very small quantities of adrenalin cause the blood pressure to sink, large quantities produce a rise. When adrenalin is given intravenously, but so slowly that the injection takes ± 1 hour the blood sugar is diminished. No details are given.—J. K.

Activity of sterilized and unsterilized ADRENALIN solutions. Wischo (F.) & Zechner (L.), Arch. Pharm., 1921, 146-149.

The authors find that a solution of adrenalin-HCl is sensitive to both light (ultraviolet) and heat; that the demand for absolutely colorless solutions is unjustified, since rose to faintly red solutions show full activity; sterilization causes no diminution but may on the contrary effect an increase in the activity of the drug.

—Chem. Abst., **16**, 787.

ADRENAL ablation in epilepsy (Nebennierenexstirpation bei Epilepsie). Wohlegmuth (K.), Fortschr. d. Med. (Berl.), 1922, **40**, 399-400.

A general review of the literature.—J. K.

(ADRENAL) Surgical pathology of hypernephroma. Wright (L.), Brit. J. Surg. (Bristol), 1922, 338-365.

With Grawitz' hypothesis (1884), that these tumours arise from suprarenal rests, the author cannot agree; amongst the facts which

militate against this contention are the following: Hypernephromata are not confined to any one area in the kidney; there is no adrenalin contained in these tumours; unlike the suprarenal tumours, alterations in sex characteristics have never been noticed in hypernephromata; no case of tumour in the suprarenal gland has ever been proved to have a papillary structure.

—Irish J. M. Sc., 1922, 5 s., 80-81.

Diagnosis of SUPRARENAL insufficiency. Wright (S.), Lancet (Lond.), 1922, **2**, 14; abst., J. Am. M. Ass. (Chicago), 1922, **79**, 505-506.

See Endocrin., 1922, **6**, 493-510.—R. G. H.

ADRENALIN tests. Zechner (L.) & Wischo (F.), Pharm. Monatsh., 1921, **2**, 141-146

The number of adrenalin tests recorded in the literature is relatively large, involving for the most part oxidizing agents capable of developing a characteristic color. The authors report results in experiments with $FeCl_3$, $KMnO_4$ and $K_2Cr_2O_7$. For adrenalin solutions 1:100 and 1:1000, the optimum concentration and amount of $FeCl_3$ solution were: 1 drop of a 50% and of 5% $FeCl_3$ solution, respectively, to 1 cc. adrenalin solution; for all lower concentrations a drop of 0.5% $FeCl_3$ solution to 1 cc. (for the concentrations 1:1,000,000 and 1:10,000,000, 6 to 10 cc.) of the adrenalin solution, making a control test with a like amount of H_2O in the case of such high dilutions. The optimum temperature for all concentrations was about 10 to 15°. One drop of a 5% $K_2Cr_2O_7$ solution added to 1 cc. of a 1:1000 solution produces a color range of yellow, orange and red, followed by a turbidity and finally brownish flakes. The turbidity does not occur with 1 drop of a 0.5% $K_2Cr_2O_7$ solution. With this strength of reagent, the test is sensitive to a 1:100,000 adrenalin solution. In the case of $KMnO_4$, 1 drop of a 0.1% solution gives a red color with adrenalin solutions, this test being sensitive in dilutions of 1:100,000.—Chem. Abst., **16**, 787.

The BASAL METABOLISM and the specific dynamic action of protein in LIVER disease. Aub (J. C.) & Means (J. H.), Arch. Int. Med. (Chicago), 1921, **28**, 173-191.

The authors conclude that the basal metabolism in twelve cases of liver disease was essentially within normal limits. The liver is therefore either not an important regulator of the metabolic rate, or it is adequate for this purpose even when severely diseased. The rate of absorption and utilization of protein in large quantities was usually normal, even in severe cirrhosis. In two cases of cirrhosis and one of gall stones, the utilization of the protein was delayed or absent. Marked portal obstruction caused no delay in the appearance of the specific dynamic action of protein. The cases of cirrhosis

showed, on the whole, the highest metabolic response to protein catabolism. The conclusion seems justified that either the liver is not the main site of the specific dynamic action of protein, or that it can adequately perform that function even in disease. The specific dynamic action of protein results from an increased combustion of protein and carbohydrate rather than fat. The observation of Du Bois that in exophthalmic **goitre** a normal increase in heat production, due to protein, is superimposed on the high basal rate is confirmed.—H. L.

Correlation of BASAL METABOLIC RATE with pulse rate and pulse pressure. Read (J. M.), J. Am. M. Ass. (Chicago), 1922, **78**, 1887-1889.

Three hundred determinations form the basis for this report. Cases showing an obvious pathologic condition in the cardiovascular-renal system are not included. A formula is offered correlating pulse rate, pulse pressure and basal metabolic rate. Pulse rate and pulse pressure vary in the same direction as the basal metabolic rate and in most individuals the change is proportionate.—W. M. A.

The pathology and treatment of DIABETES (Bemerkungen zur Pathologie und Therapie des Diabetes mellitus). Abderhalden (E.), Klin. Wchnschr. (Berl.), 1922, **1**, 1089.

In severe cases of diabetes the red corpuscles use only small quantities of oxygen. If, however, substances contained in yeast are added its use ("Sauerstoffzehrung") is largely increased. In avitaminosis the respiration of the cells (Zellatmung) is very low and yeast causes it to increase at once. Therefore, avitaminosis may perhaps play some part in causing diabetes. As the author is no clinician he suggests that medical men study this as possibly leading to useful treatment.—J. K.

(DIABETES) Variations in the blood sugar after intravenous injection of novarsenobenzol (Les variations du sucre sanguin à la suite de l'injection intraveineuse de novarsénobenzol). Achard (C.), Binet (L.) & Cournand (A.), Compt. rend. Soc. de biol. (Par.), 1922, **86**, 714-717.

Injection of novarsenobenzol in man with a normal blood sugar results in slight hyperglycemia. In diabetics and others with defective carbohydrate metabolism, it leads to a diminution of the blood sugar. Addition of novarsenobenzol to normal and diabetic bloods in vitro did not affect the sugar content.—Physiol. Abst., **7**, 251.

(DIABETES) PANCREATIC extracts. Banting (F. G.) & Best (C. H.), J. Lab. & Clin. M. (St. Louis), 1922, **7**, 464-472.

By intravenous and subcutaneous injections of neutral saline extracts prepared from the pancreas of the bovine fetus at about the

fifth month, the percentage of blood sugar and the daily urinary excretion of sugar were markedly reduced in depancreatized dogs. Daily injections of extract of pancreas enabled a depancreatized dog to live for 70 days. A small remnant of pancreas was found, however, at autopsy. The active (antidiabetic) principle of such extracts is destroyed by boiling in strongly acid reaction, but it is not affected by the presence of tricresol which may therefore be used as a preservative. The depressor action of the extract is short-lived.—R. G. H.

The liver is DIABETES mellitus. Bate (R. A.), Am. Med., 1918, n. s. **13,** 220-226.

A general article not amenable to abstracting. The author discussion various data bearing on the diabetes problem. These are largely elementary physiology and speculative endocrinology. He regards the liver and lungs as more or less similar in that both detoxicate the blood; both organs are under hormone control. In diabetes, dextrose never is stored in the liver. Trypsinogen, a hormone from the islands of Langerhans, and glycogen are always found where sugar combustion occurs. Possibly in prenatal life the **thymus** gland helps in the glycogenic function. Sugar piqûre is ineffective after **adrenal** ablation or splanchnic section. Possibly the **pancreas** hormone is neutralized by increased adrenal secretion. Then follows a review of various data on the **parathyroids, spleen** and **hypophysis.** Septic diabetes is mentioned in connection with a case of diabetes and bed-sores following fracture of the hip joint. A case of traumatic diabetes is also mentioned. For other details the original may be consulted. The therapeutic use of liver extracts in diabetes as well as in tuberculosis is advocated. At the author's request this abstract is substituted for one previously published. —R. G. H.

A case of sudden pneumonia in a DIABETIC (Un cas de pneumonie foudroyante chez une diabétique). Bonnamour & Girardot, Bull. Soc. méd. d. hôp. de Lyon, 1922; abst., Presse méd. (Par.), 1922, **30,** 620.

The authors report the case of a woman of 69 years who had had diabetes for 2 years, eliminating 3 litres of urine, with about 200 gr. of sugar and traces of acetone in 24 hours. Although supposedly on a diet, she secretly ate a great variety of food. One morning she complained of a vague stitch in her side. Auscultation was negative. The next day she was in a state of cyanosis, collapse and hypothermia. The urine contained an enormous quantity of acetone and diacetic acid. She died the next morning. Autopsy confirmed the existence of severe pneumonia.—R. G. H.

Incidence of DIABETES mellitus among Filipinos. Concepcion (I.), Philippine Islands M. Ass. J. (Manila), 1922, **2,** 57-63; abst., J. Am. M. Ass. (Chicago), 1922, **79,** 502.

Concepcion shows that the mortality of diabetes mellitus in the city of Manila has apparently been increasing within the past few years, but this is due to a greater accuracy of vital statistics. There is no reason to believe that increased consumption of sugar is one of the main factors. The incidence of diabetes in the Philippines is very much less than in other countries, including Japan, despite the use of a high carbohydrate diet. The disease is most frequent between the ages of 40 and 50 among Filipinos, Japanese and Chinese. Among Europeans it occurs most commonly between 50 and 70. The slight difference may be explained by the early maturity of Orientals as compared with Europeans. Diabetes millitus as it occurs among Filipinos is of a milder type than among Europeans and Americans. The mortality is low and only a small percentage die of diabetic coma. The low incidence of diabetes mellitus among Filipinos and other Orientals may be explained as due either to greater power of assimilation for sugar among these people compared with Europeans and Americans, or to the fact that they are less exposed to continuous nervous strain on account of their peculiar modes of living. It may also be due to some peculiar racial tendency or characteristic.—R. G. H.

(DIABETES) The influence of the phosphoric radical on blood and urine sugar in man (Die Wirkung des Phosphorsäureions auf den Blut und Harnzucker des Menschen). Elias (H.) & Weiss (S.), Wien. Arch. f. innere Med., 1922, **4**, 29-58.

Intravenous injections of hypertonic solutions of NaH_2PO_4 or Na_2HPO_4 are generally followed by a decrease of the blood sugar when this quantity is high, as in diabetes or in alimentary hyperglycemia. The normal blood sugar content is not altered, however, after these injections. When the blood sugar is high and the urine contains sugar the injections decrease the sugar in the blood for 2-4 hours and in the urine for 3 days. This is true in all cases of diabetes, whether light or serious. It is possible that this is due to an influence of phosphates on the intermedial metabolism as well as on the kidneys. Other salts do not have this effect. The bisodium salt is about twice as active as the monosodium salt. The authors first believed that this action was perhaps due to a diminished quantity of phosphorus in the blood of diabetics, but they found this quantity of phosphorus to be within the normal limits. Then a second theory was formed, namely, that the sugar partly disappeared from the blood because dextrose diphorphoric acid was made by combination of the phosphoric acid and the glucose. This seemed possible, but its existence was never proved. No influence was seen on oxydative glycolysis by the injections. No explanation of this remarkable fact could be given. (See Endocrin., 1922, **6**, 136.)—J. K.

Acetone substances in the blood in DIABETES. Fitz (R.), Tr. Ass. Am. Physicians, 1917, **32**, 154-158.

No quantitative relationship between increased concentration of acetone and lowering of blood bicarbonate was found, although in general the proportion of the acetone rose as that of the bicarbonate fell. The total acetone was increased by large amounts of fat, the maximum occurring several hours after ingestion and after visible lipaemia had disappeared. Small amounts of fat depressed blood-acetone. Fasting and pure carbohydrate diet diminished a high acetone value. $NaHCO_3$ increased the output of acetone, but its effect on blood-acetone was uncertain. In 3 fatal cases of coma, a rapid premortal rise of blood-acetone occurred; in one case this was independent of acidosis.—Physiol. Abst., **7**, 121-122.

(DIABETES) Familiar hemochromatosis (Über familiäre Haemochromatose). Frisch (A. V.), Wien. Arch. f. innere Med., 1922, **4**, 149-166.

A case of bronze diabetes is reported. The patient showed a dirty brown color of trunk and limbs and a dark brownish color of face, neck, hands and skin of scrotum and penis. The skin of the abdomen, the back and the prepuce showed many very dark pigment marks. The patient died in a diabetic coma. A very extensive postmortem report is given. **Pineal** and **thyroid** were normal, but the thyroid contained much pigment. There was cirrhosis of the **liver**, with an enormous quantity of pigment in the cells of Kupffer, in the connective tissue and in the epithelium of the bile ducts. The **pancreas** showed marked sclerosis with atrophy of the glandular parenchyma. Very few or no islands of Langerhans were found. Much pigment (hemosiderin) was found, partly intra-epithelially, partly interstitially, situated. The **spleen** contained little pigment; the follicles were atrophied; the trabeculae were partly degenerated. The connective tissue was increased. The lymph glands were very rich in pigment; in the retroperitoneal glands the lymphoid tissues had disappeared. The bone marrow was fat marrow with only a few spots of myeloid tissue; it did not contain much pigment. It was found in the mononuclear cells of the myeloid tissue, in the endothelium of the blood vessels and in the cells of the reticulum. The **adrenals** showed a normal structure; the cortex was poor in lipoid and was hyperemic. The epithelium of the glomerular zone contained much hemosiderin. The **hypophysis** contained hemosiderin, especially in the eosinophil cells of the pars anterior. The pars nervosa, too, contained much pigment. The patient had 8 brothers and sisters, who, according to him, were also pigmented. The two brothers seen by the author were pigmented and had an indurative sclerosis of the liver, but no diabetes. Formerly there were many theories as to the relations between pigment and diabetes. It is now generally accepted that hemochromatosis is a predisposition to diabetes. That this theory is true is proved by this case in which two brothers do not have diabetes, but have all the other

symptoms of bronze diabetes. The author believes that cirrhosis of the liver as well as diabetes is due to hemachromatosis. He accepts the theory of Eppinger that in hemosiderosis the endothelium elements of the body have lost their power to change the iron into a substance that the other cells of the body want. If this theory is true,—that bronze diabetes is a disease of the complete endothelial apparatus of the body,—it belongs to the same class as splenomegaly of Gaucher or hemolytic icterus. There are two types of hemolytic icterus, the familial type (Minkowski) and the individual type (Hayem). These cases of hemochromatosis prove that here, too, not a congenital but a familial and an individual type exist.—J. K.

DIABETES in negro: Report of eight cases. Goldstein (H. I.), New Jersey Med. Soc. J. (Orange), 1922, **19**, 157.

Eight cases of diabetes in the negro are reported by Goldstein in a series of 65 cases of diabetes mellitus. Apparently, diabetes in the negro is much less common than in the white population. Syphilis is not an important causative factor in negro diabetics.
—J. Am. M. Ass., 1922, **79**, 329.

(DIABETES) Glycemia and glycosuria. Graham (G.), Lancet (Lond.), 1921, **1**, 1002-1007.

This is the second of a series of three lectures by the author on this subject. It deals primarily with the various conditions under which sugar is excreted in the urine. Sugar may appear in the urine in other conditions than in diabetes mellitus, and other sugars than glucose frequently are found. In such cases there is excretion of copper sulphate reducing substances without symptoms of diabetes. No treatment is required for cases of diabetes innocens or renal diabetes. The sugar tolerance test is employed to confirm the diagnosis of diabetes mellitus when sugar is found in the urine. It is pointed out also that the "leak point" or kidney threshold is very low in non-diabetic cases of glycosuria, sugar often being found in the urine when the blood sugar is normal. The author is of the opinion that the increased elevation of the renal threshold often found in diabetes is a defensive mechanism.—I. M.

(DIABETES) Glycemia and glycosuria. Graham (G.), Lancet (Lond.), 1921, **1**, 1059-1065.

This is the third of a series of three lectures on this subject. The various hypotheses advanced to explain the cause of diabetes and the modern types of diabetic therapy are considered. A brief but comprehensive discussion of the literature on the pathology of diabetes is included. The author then describes experiments made by himself on two severe cases of diabetes in which he found sodium bicarbonate therapy to be of value because it increased the alkali reserve and because it caused increased elimination of acetoacetic

acid. The latter substance the author, like Hurtley and Trevan, believes is the cause of coma in diabetes. Neutral acetoacetates when given to animals intravenously in large doses cause symptoms of coma. This indicates that it is not the added H-ions of the acetoacetic acid that cause diabetic coma and explains the failure of alkali therapy in this condition.—I. M.

Functional tests in DIABETES. Offenbacher (R.) & Hahn (A.), Arch. f. Verdaungskr. (Berl.), 1922, **29**, 318.

This communication from Strauss' service emphasizes that a single record of the blood gives no reliable information as to the normal or abnormal character of the carbohydrate metabolism. This can be estimated with precision from the behavior of the sugar content of the blood during the first three hours or more after ingestion, fasting, of 50 gm. of glucose in 300 cc. of tea. With true diabetes, the glycemia does not rise to its peak until the second or third hour, and sugar always appeared in the urine. The details of nine cases of diabetes, free from glycosuria at the time, are tabulated. From 0.125 the glycemia ran up to 3.36 in the second hour in one case, and the reaction was evident for three hours. If the glycemia after the peak in the second hour returns promptly to normal, then the disturbances can be ascribed to neurasthenia or endocrine factors. If it lasts longer than this, a true disturbance of the intermediate sugar metabolism seems certain.

—J. Am. M. Ass., **78**, 1934.

The acetonuria of DIABETES. Hubbard (R. S.) & Nicholson (S. T. Jr.), J. Biol. Chem. (Balt.), 1922, **53**, 209-230.

A method has been described for calculating a molecular ratio between ketogenic and antiketogenic compounds contained in the diet which is applicable to diabetic patients, and 7 cases have been described in which a comparison was made between the values of this ratio and the excretion of the acetone bodies in the urine. It has been shown that the acetone excretion varies inversely with the numerical values of this ratio. A study of the numerical values of the ratio calculated for the diets which correspond with a slightly increased excretion of acetone shows that they were approximately the same as those values found for normal subjects receiving diets low in carbohydrate, but containing sufficient calories to supply the needs of the subject. It has been shown that fat fed sometimes increases the amount of acetone excreted, even when the increase replaces a part of the fat which the body was probably withdrawing from its own reserve supplies of this material.—F. S. H.

The chemistry of DIABETIC glucosuria. Ionescu (A.), Bull. soc. chim. Rumania, 1921, **3**, 97-104.

A discussion of the chemistry of the diabetic organism chiefly of theoretical interest.—Chem. Abst., **16**, 1620.

Clinical aspect of studies on the metabolism of DIABETES. Joslin (E. P.), Tr. Ass. Am. Physicians, May 2-4, 1922.

Prior to the introduction of treatment by undernutrition, the average urinary nitrogen excreted per kilogram of body weight for 24 hours was 0.265 gm. After that time, for a considerably larger series of cases, the average urinary nitrogen excretion was 0.185 gm. per kilogram of body weight for the 24 hours. The average metabolism for the early series was + 12 per cent and for the later series — 11 per cent. Comparison of the urinary nitrogen determinations with loss in body weight with metabolism and with the respiratory quotient suggest that protein metabolism alone does not control the total metabolism; that exogenous protein may be more stimulating to the metabolism than endogenous protein; that a very high nitrogen excretion in a severe diabetic may represent the prelethal rise, and that even such a diabetic may have the power to oxidize carbohydrate to a degree which is often not appreciated, but obviously should be utilized.—J. Am. M. Ass., 1922, **79**, 71.

The treatment of DIABETES by the general practitioner. Joslin (E. P.), Penn. M. J. (Harrisburg), 1922, **25**, 373-381.

A splendid concise summary of modern methods in treating diabetes mellitus, with an appeal to the country practitioner and city internist to familiarize themselves with these advances. The author's well known tables of food values and diabetic diets illustrate the article, which greatly help to simplify the arithmetic of modern diabetic dietetic therapy. Test diets, and maintenance diets are explained; the prevention of diabetes, causes of death in diabetes, treatment of diabetic acidosis, gangrene and infections, surgery in diabetes, indications and values of blood sugar determinations are all tersely reviewed.—H. L.

Today's problem in DIABETES in light of nine hundred and thirty fatal cases. Joslin (E. P.), J. Am. M. Ass. (Chicago), 1922, **78**, 1506-1510.

This is a statistical study of the progress in treating diabetes by Allen's method as compared with the years before the adoption of treatment by undernutrition. A brief exposition of the test and maintenance diets as used by the author is also presented. The article is not suited to more detailed abstraction.—W. M. A.

(DIABETES) The action of heterogenous proteins on the organism. Heterogenous proteins and glucose in the blood (Recherches sur l'action des protéines hétérogènes dans l'organisme. Protéines hétérogènes et glycose dans le sang). Lüttichau (A.),

Arch. internat. de physiol. (Liége & Par.), 1922, **19**, 1-15; abst., Physiol. Abst., 1922, **7**, 250.

The intravenous injection of small quantities of certain proteins (ovoglobulin, but not ovalbumin, saliva, and casein) causes hyperglycemia, but not glycosuria in dogs; ½ to ⅓ of the proteins injected can pass out in the urine. Since the injection of the white of egg has a lymphagog, hepatic action, it is supposed that in the case of ovoglobulin there is also excitation, due to the formation of glucose in the liver, rather than a diminution in the consumption of the glucose. The author uses these experimental data in the discussion of the mechanism of glycosuria which is sometimes seen after the ingestion of proteins in persons with diabetes but not glycosuria.—R. G. H.

Effects produced on DIABETES by extracts of pancreas. Macleod (J. J. R.), Banting (F. G.), Best (O. H.), Collip (J. B.), Campbell (W. R.), Fletcher (A. A.) & Noble (E. C.), Tr. Ass. Am. Physicians, May 2-4, 1922.

Researches on the action of pancreatic extracts have hitherto failed to take into account that there might be a powerful proteolytic enzyme which could destroy or digest any internal secretion also present. The authors have sought to obtain the pancreatic secretion isolated from such a proteolytic ferment, and to study its independent action. A highly potent product was obtained in small quantities from cattle fetus pancreas, which was termed "insulin." This is harmless to man and to laboratory animals when given in proper dosage, but toxic in large proportions. In 7 cases of human diabetes mellitus, subcutaneous injection of insulin reduced the blood sugar to normal level with disappearance of sugar and ketone bodies from the urine. The improved carbohydrate metabolism was evidenced by improvement in the respiratory quotient, which rose decidedly within two hours, while the patients felt a marked improvement in symptoms and in general well being. Laboratory experiments indicate that the pancreatic extract employed contained properties controlling carbohydrate and fat metabolism, yet its clinical results cannot be estimated. Probably the dietetic treatment will still be foremost, but the extract promises to be of value in tiding the patient over those crises which are frequently uncontrollable by other means.—J. Am. M. Ass., 1922, **79**, 71.

(DIABETES) Organ stimulation by roentgen ray. Petersen (W. F.) & Saelhof (C. C.), J. Radiol. (Omaha), 1922, **3**, 135-138.

Experiments were carried out by the authors upon depancreatized dogs and the general conclusions drawn were that with moderate doses of roentgen rays applied over areas containing pancreatic rests there may result an augumentation of sugar excretion, followed by evidence of pancreatic stimulation with increased

sugar tolerance lasting from three days to three weeks. If the dose was too large or if a cumulative effect was produced there resulted a lowering of the sugar tolerance. Conditions for this type of experiment are much more favorable in the dog than in the human diabetic subject, but even in clinical cases there is some evidence that a diabetic process may be influenced by direct radiation; though such treatment is not advised in diabetic coma at present unless all other means prove of no avail.—R. G. H.

Syphilitic origin of DIABETES (L'origine syphilitique du diabète). Pinard (M.), Bull et mém. Soc. méd. d. hôp. de Par., 1921, **45**, 760-765.

Pinard, investigating the history of 23 cases of diabetes, found that 10 showed evidence of old acquired syphilis and 5 of hereditary syphilis; of the remaining 8 no inquiry for syphilis had been made. He mentions cases in which sugar disappeared in the urine during treatment with salvarsan and reappeared afterwards. He also mentions that Warthin found syphilitic lesions in six cases of diabetes, although they were unsuspected during life. Pinard concludes that syphilis, acquired or hereditary, is an important cause of diabetes, which may be due to **pancreatic, hepatic, hypophyseal,** or bulbar lesions, and that syphilitic diabetes may be benefited by antisyphilitic treatment. Other observers, however, find evidence of syphilis in a smaller percentage of cases of diabetes. Thus Rosenbloom, in 139 cases of diabetes mellitus, found a positive Wassermann reaction in about 12 per cent. Intensive treatment had no effect in increasing tolerance for carbohydrates. He concludes that in about 6 per cent the diabetes was syphilitic in origin, and in about 6 per cent independent of syphilis. He quotes other observers as having obtained similar percentages.—Med. Sc., 1922, **6**, 187-188.

(DIABETES) The practical importance of the alimentary hyperglycemia curve (Über die praktische Bedeutung der alimentären Hyperglykamie-Kurve). Rosenberg (M.), Klin. Wchnschr. (Berl.), 1922, **1**, 360-362.

The relation between the sugar in the blood and in the urine is extremely complicated. Comparatively small doses of glucose cause glycosuria when they are not given by mouth but by the rectum, so that they need not pass the liver. The author gave 100 gm. of glucose to healthy persons and constructed an average normal blood sugar curve. In diabetes the blood sugar rises higher than in normal persons and it may be much longer before the original blood sugar content is reached. This seems to be an excellent way to diagnose between very light cases of true and of renal diabetes. In **Graves' disease** the curve is sometimes quite normal, even in extremely serious cases. In other cases it closely resembles the curve in diabetes.—J. K.

(DIABETES) Blutzuckerstudien. I. Kritik der Blutzuckerbestimmungsmethoden. Rosenberg (H.), Arch. f. exper. Path. u. Pharmakol. (Berl.), 1922, **92**, 153-164.

A critical account of previous studies on the blood sugar.
—Physiol. Abst., **7**, 250.

Blood pressure studies in 140 cases of DIABETES mellitus. Rosenbloom (J.), J. Lab. & Clin. M. (St. Louis), 1922, **7**, 392-399.

One hundred and forty cases of diabetes mellitus studied by Rosenbloom showed that the blood pressure in uncomplicated diabetes is normal or slightly under normal. In every case in the series where there was present a high blood pressure it could be demonstrated that an existing nephritis, arteriosclerosis or aortitis was present. In this series 22 cases of diabetes were complicated by hypertension—a percentage of about 16. The presence or absence of sugar in the urine had no effect on the blood pressure. A high blood pressure in diabetes is due to a chronic nephritis, arteriosclerosis or a cardiac hypertrophy.—R. G. H.

The chemical procedures that are of use in the control of DIABETES. Snowden (R. R.), Penn. M. J. (Harrisburg), 1922, **25**, 383-389.

The author considers the glucose content of the blood indispensable in the diagnosis and study of a diabetic. It is always above normal in a diabetic who is excreting sugar in the urine and not infrequently is above normal even when the urine is sugar free. Treatment, therefore, should be based on the blood sugar rather than the urinary tests. An accurate measure of the degree of acidosis can be obtained by measuring the alkaline reserve, and sometimes approaching acidosis can be detected before this is evident from the clinical picture.—H. L.

(DIABETES) Sugar metabolism in man (Studien uber den Zuckerstoffwechsel des Menschen). II & III. Staub (H.), Ztschr. f. klin. Med. (Berl.), 1922, **93**, 89-123; 123-140; Klin. Wchnschr. (Berl.), 1922, **6**, 1332.

It is found that after a meal followed 10-15 hours later by the administration of 20 gm. of glucose dissolved in 100 cc. of water there is little rise of the blood sugar. When the time between the meal and the administration of glucose is more or less than 10-15 hours, there is greater increase of blood sugar. Staub was able to prove that a comparatively small rise of blood sugar and a short duration of this hyperglycemia after the ingestion of 20 gm. of glucose was a sign of good carbohydrate assimilation, while long duration and high hyperglycemia are found when this assimilation is defective. Thus it may be concluded that assimilation of carbohydrates reaches its minimum after 10-15 hours of starvation. The changes in carbohydrate metabolism during starvation are probably

due to changes in the formation of enzymes which act upon the intermedial sugar metabolism. The formation of these enzymes depends both upon the quantity of carbohydrate in the body and those taken by mouth. When glucose is given during strenuous work the hyperglycemia is much less intense than when the person is at rest. After ingestion of glucose during work the hyperglycemia becomes hypoglycemia at the moment at which the person at rest has a maximum hyperglycemia. In a person with a normal dose of glycogen in his body the influence of glucose on the blood sugar during moderate work is the same as during rest; moderate work has the same influence on a person with a small quantity of glycogen as strenuous work has on a normal organism. When a person takes only fat and proteins for two days the rise of blood sugar after the ingestion of glucose is higher than when he has taken carbohydrates for two days.—J. K.

Causes of DIABETES (Feststellungen zur Diabetesätiologie). Strauss (H.), Klin. Wchnschr. (Berl.), 1922, **1**, 885-887.

From the beginning of the war until the autumn of 1916, 1524 cases of diabetes were seen in the German army. In 70 cases the disease was caused by trauma; in 45 cases diabetes was seen after infection; 10 cases probably were due to shock. Of the other cases no details are known. Of these 1524 cases, 909 or 72.8% became diabetic during the war. Among the 70 traumatic cases, there were only 5 wounds of the skull. Among the infectious cases (45), 17 were due to dysentery, 4 to enteritis, 4 to typhoid fever, 3 to cholera and 2 to paratyphus. Enteric infections seem to play an important rôle.—J. K.

(DIABETES) A comparison of several clinical quantitative blood sugar methods. Thalhimer (W.) & Updegraff (Helen), J. Am. M. Ass. (Chicago), 1922, **78**, 1383-1388.

The Benedict, the Myers and Bailey modifications of the original Lewis and Benedict method, and the latest modification of the Folin and Wu method for blood sugar determination are compared as to normal values and as to accuracy. The normal values are distinctly different by the three methods, so that it is necessary to report the method when giving a blood sugar estimation.—W. M. A.

Postoperative pancreatic DIABETES. Umber, Klin. Wchnschr. (Berl.), 1922, **1**, 1232.

One-half year after an operation for a cyst of the pancreas the patient developed diabetes. Details are not given.—J. K.

Estimation of sugar in DIABETIC blood. Vigevani (G.), Boll. Chim. Farm., 1919, **58**, 436-439.

Two cc. of the blood are mixed with 100 cc. of KCl solution (saturate KCl solution 340 cc., HClO 375 cc., and water 160 cc.);

50 cc. of the mixture are boiled for 5 minutes, filtered from the precipitated proteins, the filtrate is made up to a definite volume, and 10 cc. are introduced into an Erlenmeyer flask, around the neck of which rubber tubing has been fixed. From 1 to 2 cc. (according to the amount of dextrose) of a Cu solution (Cu SO_4 2.2, $KHCO_3$ 80, $K_2CO_3$50, KCl 53 g., water, 500 cc.) are added, the mixture is boiled for 3 minutes, and the rubber tube closed with a clip, so that after cooling a vacuum is produced within the flask. A current of CO_2 is then introduced and the liquid titrated with I solution (0.1 NHCL 5 cc., I 0.0635 g., KI 2 g., 2% KIO_3 solution 2 cc., and water to 100 cc.) with starch solution 2 g. soluble starch in 100 g. of saturated KCl solution as indicator. The Cu reduced by the dextrose reacts with the I solution. The latter is previously standardized on pure dextrose which has been dried at 100°.—Chem. Abst., **16**, 1260.

(DIABETES mellitus) The opthalmologists' standpoint. Weisser (E. A.), Penn. M. J. (Harrisburg), 1922, **25**, 381-383.

With the exception of diabetic cataract, eye symptoms in diabetes are more frequent, according to Weisser, where this disease is of long duration, and when it occurs mostly late in life, between 50 and 70 years of age. Diabetic cataracts affect both sexes equally, are usually binocular, very rapid in growth and soft in character. The treatment is operative just as in senile cataract. The dangers are slow healing, inviting infection, iritis and hemorrhage, followed by secondary glaucoma. Diabetic retinitis occurs late in the disease, is usually accompanied by some loss of visual acuity and changes in the vitreous with little hope of regaining any of the vision lost. Diminution in the range of accommodation, probably from some toxic action of glucose, is usually relieved by the elimination of sugar. Changes in refraction occur, usually myopia, and often cured by dietetic treatment. Diabetic amblyopia occurs occasionally and vision slowly improves under proper dietetic treatment. Extra-ocular paralyses may be due to diabetes, especially diplopia and ptosis.—H. L.

Optimal food mixtures for DIABETIC patients. Wilder (R. M.), J. Am. M. Ass. (Chicago), 1922, **78**, 1878-1884.

A satisfactory dietary should embody four principles: (1) total dietary restriction, (2) protein restriction, (3) carbohydrate restriction, (4) balanced fat and carbohydrate. These principles are discussed and charts and formulas are given for calculating the optimal diet.—W. M. A.

(DIABETES) The threshold of ketogenesis. Wilder (R. M.) & Winter (M. D.), J. Biol. Chem. (Balt.), 1922, **52**, 393-401.

Another paper built on assumptions which are employed in the calculation of the composition of the mixture of food substances

engaging in metabolism. Under the conditions of the experiments reported here on man, providing the assumptions are tenable, the ratio between the ketogenic and the glucose molecule at which a clinically significant ketosis appears has a value of at least 2:1. A ratio of this value implies that every molecule of glucose is ketolytic for 2 molecules of acetoacetic acid. The existence of infection lowers the ketogenic threshold so that siginficant ketogenesis may occur with lower ratios. Other factors, thus far undetermined, may also lower this threshold. It is advisable, therefore, in planning diets for diabetic patients to allow only such food mixtures as will avoid the 2:1 ratio by a safe margin.—F. S. H.

Objects and method of diet adjustment in DIABETES. Woodyatt (R. T.), Arch. Int. Med. (Chicago), 1921, **28**, 125-141.

Woodyatt reconciles and explains the confusion from such conflicting diets as the Falta "cereal cure," Donkin "milk cure," von Duering "rice cure," Mossé "potato cure," von Noorden "oatmeal cure," and recent low protein high fat diets of Newburgh and Marsh. He takes exception to the universal necessity or wisdom of the "total dietary restriction" and "undernutrition" regimes of Allen and Joslin. He points out that the quantity of oxidizing glucose fixes an upper limit to the quantity of ketogenic fatty acid that can be completely oxidized at the same time. The ratio of higher fatty acids to glucose, which if exceeded will lead to acidosis, is likely to be close to 1.5 to 1 (in gm.). In diets below maintenance, the body tissues will be burned, and if the patient is fat, he will burn fat and but little protein, but if he has but little fat, he will utilize considerable body protein which means .58 glucose. This will hold down the amount of glucose that can be given in the diet as carbohydrate and protein. But if sufficient fat is given in the diet to prevent catabolizing of body protein, more glucose can be given in the diet—a higher caloric intake obtained and a better state of nutrition result. These principles are worked out mathematically and equations and ratios given. A practical example is included of a case in which these principles and methods were followed out systematically with most interesting and satisfying results.—H. L.

Confusion of methanol poisoning with DIABETES. Zeigler, Brit. J. Ophthalmology; Am. J. Public Health, 1921, **11**, 1115.

It is noted that the end product excreted by the kidneys is formic acid and that this reduces Fehling solution so that a wrong diagnosis is possible.—Chem. Abst., **16**, 1278.

Experimental DIABETES INSIPIDUS. Bailey (P.) & Bremer (F.), Arch. Int. Med. (Chicago), 1921, **28**, 773-803.

In order to throw further light on the pathogenesis of diabetes insipidus, systematic punctures of the hypothalamus were made in 23 adult dogs, employing the lateral route of Paulesco and Cushing,

giving perfect exposure, and avoiding any injury of the **hypophysis.** It was found that a lesion, even extremely minute, of the para-infundibular region of the hypothalamus provokes with certitude polyuria, which appears in the first two days and, according to the extent of the lesion, is transient or permanent. In the latter case cachexia "hypophyseopriva," genital atrophy and adiposity are present. Permanent polyuria has all the characteristics of diabetes insipidus in man, e. g., possibility of concentration when intake of fluids is restricted, when pituitary extract is injected subcutaneously, or in the presence of fever. Thirst may precede polyuria. Experimental diabetes insipidus does not depend on a disturbance of a supposed nervous or vascular regulation of the kidney, proven by its production in animals whose kidneys have been denervated. Lesion of the tuber cinereum produced in two dogs a **cachexia "hypophyseopriva"** with acute genital atrophy and in two other dogs an insidiously developing **adiposogenital dystrophy.** The integrity of the pituitary was in each case verified histologically. The same dogs had persistent polyuria.—H. L.

Considérations sur la pathogénie du diabète insipide et du syndrome adiposo-génital. Bremer, III Réunion neurol. internat. ann., Paris, 1922; abst., Presse méd. (Par.), 1922, **30,** 605.

See Endocrin., **5,** 761-762.—R. G. H.

DIABETE insipide syphilitique avec hémianopsie bitemporale et crises de narcolepsie. Foix, Alajouanine & Dauptain, III Réunion neurol. internat. ann., Par., 1922; abst., Presse méd. (Par.), 1922, **30,** 615.

The authors report a case of infundibular syndrome analogous to that described by Claude and Lhermitte in a case of tumor of the third ventricle. The diabetes insipidus persisted in spite of antisyphilitic treatment.—R. G. H.

Renal GLYCOSURIA. Marsh (P. L.), Arch. Int. Med. (Chicago), 1921, **28,** 54-61.

A case of renal glycosuria is described. During a period of four months the patient excreted an average of 60 gm. glucose daily with a variation of from 15 to 122 gm. The amount was not related to the carbohydrate intake. Diuresis by increased water ingestion caused no increase in the glycosuria, and no effect was seen from the administration of diuretin in large doses. No evidence of nephritis was found. The blood sugar curve was normal.—H. L.

DIABETES INSIPIDUS. Mikus, Klin. Wchnschr. (Berl.), 1922, **1.** 1131.

Demonstration of a patient with **syphilitic** diabetes insipidus and changes in the bones of the sella. Antisyphilitic treatment diminished polyuria and polydypsia, though the specific gravity of the

urine remained very low. In the last months, however, the patient began to show symptoms of osteomalacia.—J. K.

Metabolic studies on a case of DIABETES INSIPIDUS. Rabinowitch (I. M.), Arch. Int. Med. (Chicago), 1921, **28**, 355-366.

A man, aged 47, was carefully studied in the Montreal General Hospital; his was the only case of diabetes insipidus in the last 50,000 admissions. The blood chemistry was as follows:

Non-protein nitrogen	28.0	mg. per 100 cc.;
Urea nitrogen	16.0	mg. per 100 cc.;
Uric acid	1.1	mg. per 100 cc.;
Creatinin	1.2	mg. per 100 cc.;
Cholesterol	0.126	mg. per 100 cc.;
Sugar	0.100	per cent;
Chlorids (as sodium chlorid)	0.627	per cent (plasma);
Total protein	7.4	per cent;
Albumin	4.6	per cent;
Globulin	2.8	per cent.

The only abnormal finding was the hyperchloremia. Basal metabolism estimation showed a normal rate. The Goetsch test and Csepai conjunctival test were negative, suggesting hypofunction of the **suprarenals.** The Ascoli subepidermal test was only slightly positive. There was diminished sugar tolerance, suggesting **hyperpituitarism.** The Mosenthal renal test meal showed faulty metabolism of salt and water. The kidneys were unable to excrete chlorids properly. Rabinowitch concludes that in his case no single specific lesion was found to account for the polyuria. An endocrine and a renal factor were present. Pituitary extract improved not only the concentration, but also the rate of excretion, suggesting that diabetes insipidus is caused by a lack of some internal secretion which normally regulates and moderates diuresis by acting on the renal cells.—H. L.

A case of DIABETES INSIPIDUS with consideration on the mode of action of extract of the posterior lobe of the HYPOPHYSIS (Un cas de diabète insipide avec considérations sur le mode d'action de l'extrait de lobe postérieur d'hypophyse). Souques, Alajouanine & Lermoyez (J.), III Réunion neurol. internat. ann., Paris, 1922; abst., Presse méd. (Par.), 1922, **30**, 615.

A case is described of a young girl with diabetes insipidus of unknown etiology and with polyuria of 16 litres. The renal function was normal. The influence of extracts of the posterior lobe of the hypophysis was remarkable, but lasted only 8-10 hours. A series of experiments to decide the mode of action of these extracts did not determine whether the pars intermedia or the pars nervosa played the principal rôle. Renal polyuria was affected and even in normal subjects the action was that of a medicament rather than of organotherapy.—R. G. H.

DIABETES INSIPIDUS. Umber, Klin. Wchnschr. (Berl.), 1922, **1**, 1232.

A short note. The patient had hemianopsia and polyuria. The skiagram showed no changes in the sella. As the Wassermann test was positive, antisyphilitic treatment was given. The patient is completely cured.—J. K.

(ENDOCRINE ORGANS) Further studies on substances with specific action prepared from single organs. VII. Chemotactic experiments on Paramecia and experiments on the velocity of their division under the influence of optones from different organs (Weitere Untersuchungen über die von einzelnen Organen hervorgebrachten Substanzen mit spezifischer Wirkung. VII. Chemotaktische Versuche an Paramaecien und Untersuchungen über die Geschwindigkeit ihrer Teilung unter dem Einfluss von Optonen aus verschiedenen Organen). Abderhalden (E.) & Schiffmann (Olga), Arch. f. d. ges. Physiol. (Berl.), 1922, **194**, 206-217.

Optones from the **corpus luteum, pituitary, ovary, thyroid** and **thymus,** diluted 1:100 act fatally, or negatively chemotactic on paramecia; still greater dilutions show positive chemotaxis. Specific actions of single optones cannot be observed. Optones from thymus, **testis,** and thyroid increase the intensity of division, while those from pituitary and corpus luteum retard it. The retardation from pituitary is overcome by repeated treatment.—A. T. C.

Action of extracts of the ENDOCRINE GLANDS upon the isolated uterus, particularly after castration (Action d'extraits et produits dérivés d'organes à sécrétion interne sur l'utérus isolé, particulièrement après le castration totale). Athias (M.), Arch. internat. de pharmacad. et de thérap. (Gand. & Par.), 1921, **25**, 423-452.

A confirmation of the results of previous workers on the response of the isolated uterus of different species to extracts of the **pituitary** and **suprarenal** glands. Rhythmic contractions disappear after castration, but otherwise the behavior is normal after this operation. A reversal of the **adrenalin** effect after pituitary was not obtained.—Physiol. Abst., **6**, 327.

(ENDOCRINE) The calcium content of the blood in guanidine poisoning (Über den Calciumgehalt des Blutes bei der Guanidinvergiftung). Bayer (G.), Ztschr. f. d. ges. exper. Med. (Berl.), 1922, **27**, 119-126.

Guanidine poisoning causes in rabbits, cats, and guinea pigs in a few hours a decrease of the Ca ions in the blood. This decrease is usually smaller than after the extirpation of the **parathyroids,** but it may be as high.—Physiol. Abst., 1922, **7**, 257.

(ENDOCRINE) Pathogenesis of congenital fragilitas ossium [Beitrag zur Kenntnis der Pathogenese der Fragilitas ossium congenita (Osteopasthyrosis infantiltis)]. Bolten (G. C.), Deutsche Ztschr. f. Nervenh. (Leipz.), 1919, **63**, 343-359.

Reports of three cases of fragilitas ossium. Two patients were brothers, aged 18 and 11 years respectively; the third was a 3 year old girl. All were from neuropathic families, and showed blue sclerae, very fragile bones and various vasomotor-trophic disturbances, for example, frequent attacks of urticaria, cold, clammy hands and feet, etc. Bolten believes that this condition is the result of disturbances in the trophic function, and that this has its cause in a hypotonia of the vegetative (especially of the sympathetic) nervous system and of the therewith functionally inseparable "accelerating glands of internal secretion." In addition to the above clinical observations, Bolten thinks that his view is supported by two arguments, namely, (1) that there were very many manifestations of sympathetic hypotonia present not only in the three patients, but also in the mother and other brothers and sisters of the first two patients; and (2) that in the family of the third patient there was a remarkably large number of cretins and also manifestations of vagotonia.—J. P. S.

(ENDOCRINE) Vasomotor neurosis cured (Die vasomotorische Neurose Nothnagels). Bolten (G. C.), Deutsche Ztschr. f. Nervenh. (Leipz.), 1921, **70**, 256-265.

This is a report of a case in a woman 52 years old. The condition was characterized by paresthesias; pains, especially burning pain, in different parts of the body; sensory disturbances, hyper- and hypo-esthesias; and vasomotor disturbances. Such cases usually occur in females about the time of the menopause. Bolten, therefore, thinks that failure of the internal secretion of the **ovaries** plus disturbances of the **adrenal** lead to hypotonia (vagotonia). This patient improved on small doses of ovarian, **thyroid** and adrenal preparations. When the patient stopped the medication for a time the paresthesias returned, to disappear again on resuming the treatment.—J. P. S.

(ENDOCRINE ORGANS) Neurological metabolism of the medulla oblongata. II. Experiments on the regulation of the carbohydrate metabolism in the oblongata (Zur Stoffwechselneurologie der Medulla oblongata. II. Experimenteller Beitrag zur Regulation des Zucherstoffwechsels in der Oblongata). Brugsch (T.), Dresel (K.) & Lewy (F. H.), Ztschr. f. d. ges. exper. Med. (Berl.), 1921, **25**, 262.

It was previously shown that the piqûre point in the 4th ventricle is identical with the sympathetic-vagus nucleus. Stimulation thereof did not always induce hyperglycemia. Examination of serial

sections of the place of injury now shows that when the posterior 3rd was touched hyperglycemia resulted. When the anterior half was stimulated a hypoglycemia ensued. The anterior half sets the **suprarenals** in action, the posterior portion controls the vagus fibres to the **pancreas**.—Physiol. Abst., **7**, 97.

(ENDOCRINE) Roentgenological findings in Mongolism. Clift (M. W.), Am. J. Roentgenol. (N. Y.), 1922, **9**, 420-422.

The author takes issue with Timme, who has reported a characteristic sella turcica picture in Mongolism. In Clift's opinion there is no single characteristic roentgenological sign in this disease, and the only departure from normal is a generalized delay of bone development. This feature, except for a slight selective character on the part of the nose and maxilla, is common to a number of other diseases, some of endocrine origin and others due to obscure causes.

—R. G. H.

(ENDOCRINE) Insuffisance pluriglandulaire fruste et troubles mentaux chez un hérédo-syphilitique avec rhumatismes chroniques ankylosants post-infectieux. Cornil & Robin (G.), Soc. clin. de méd. mentale, May 15, 1922; abst., Presse méd. (Par.), 1922, **30**, 481.

The authors describe a hereditary syphilitic who had, at 9 years, a meningeal infection, complicated by cervical spondylosis, ankylosis of the hips and radiocubital synostosis, and recently by epilepsy and mental disorders. Due to the insufficiency of the **thyroid, testicle** and **hypophysis**, the authors believe these troubles to be caused in most cases by hereditary syphilis, though there is the possibility of pluriglandular insufficiency from general infection.

—R. G. H.

Glandular adipose tissue and its relation to other ENDOCRINE ORGANS and to the vitamine problem. Cramer (W.), Brit. J. Exper. Path. (Lond.), 1920, **1**, 184-196.

As a result of experimental work, mostly on white rats and tame mice, but also with the perinephric fat of the guinea pig, rabbit and man, the author concludes that in all these forms there exists a glandular type of adipose tissue (variously known as "brown fat," "hibernating gland," etc.), which is histogenetically and functionally distinct from ordinary adipose tissue, although in most species it acquires the appearance of ordinary adipose tissue soon after birth. Stress is laid upon the fact that the fatty material of this glandular adipose tissue is rich in cholesterin compounds and other lipoids in addition to true fat, and that these lipoids are largely retained during ordinary starvation but are used up in animals dying from having been on a vitamine-free diet. With this loss of lipoid, the tissue comes to resemble a very vascular endocrine organ. Possibly the lipoid has been used up to supply vitamines. Since vitamine deficiency also causes great loss of lipoid from the suprarenal cortex

and since there is great similarity in the reaction to polarized light between the **adrenal** cortex and this glandular adipose tissue, the author assumes that there is also great similarity in composition between these two tissues. The glandular adipose tissue may also be closely related to the function of the **thyroid** since the fatty accumulations in cretins have by some been considered enlargements of this glandular type of adipose tissue. The conclusion is that disturbances of the functional activity of this glandular adipose tissue will have to be taken into consideration in connection with deficiency diseases. "Lipoid gland" or "cholesterin gland" is suggested as a better name for this tissue.—A. T. R.

(ENDOCRINE) Sterility. Forsdike (S.), Practitioner (Lond.), 1922, **108**, 243-251.

Sterility in the female may be due to persistence of undeveloped organs; altered secretions of the genital tract (infectious); gross lesions of the tract (tumors or trauma); functional causes, vaginismus, metabolic changes or changes of the internal secretions; or failure of **ovulation.** Nothing further of endocrine interest is included.—H. L.

The ENDOCRINE system: some relations to ophthalmology and otolaryngology. Fridenberg (P.), Penn. M. J. (Harrisburg), 1922, **25**, 523-527.

The profound influence of the ductless glands upon the structural development and function of the entire body obviously suggests a relationship ofttimes to anomalies of development and derangements of function in the domain of ophthalmology and otolaryngology. The author suggests that **hyperthyroidism** may lead either to exophthalmos or glaucoma, depending on whether the eye structure is vagotonic in type. The latter is characterized by a stiff sclera, large lens, small pupil, ripe for an acute attack of glaucoma if there is an excessive sympathicotonia as in hyperthyroidism. Fridenberg distinguishes two endocrine ocular types. The **pituitary** eye is recessed, enophthalmic, with small lid fissure, contracted pupil and tendency to marked pigmentation and hyperopic refraction. The hyperthyroidic eye shows exophthalmos, mydriasis, large lid fissure, vascularity of conjunctiva and lids, and a tendency to epiphora, subnormal accommodation, defective convergence and the various asthenopias.—H. L.

ENDOCRINE glands and their importance in tropical pathology (Nociones sobre las glandulas endocrinas y su importancia in la patologia tropical). García de Quevedo (L.), Bull. Porto Rico Med. Ass., 1922, **16**, 65-73.

A general summarizing discussion of present day endocrinology, not amenable to abstracting.—R. G. H.

(ENDOCRINE ORGANS) Dwarfism and gigantism (Über Zwergwucks und Riesenwuchs mit einem Beitrag zum Studium verwandter Entwicklungstörungen im Organismus). Gigon (A.), Schweiz. Arch. f. Neurol. u. Psychiat. (Zürich), 1921, **9**, 283-302; 1922, **10**, 113-129.

This article includes the history, physical findings, x-ray findings, etc., in 10 cases of abnormally small or unusually large patients with a discussion of their classification and the involvement of the ductless glands, with the conclusion that there is great need for new clinical investigations on such morphological characters as skeletal form, adiposity, mammary glands, hirsute, etc. Ninety-eight references are given.—A. T. R.

(ENDOCRINE ORGANS) The influence of the nervous system on adipose tissue (Über den Einfluss des Nervensystems auf das Fettgewebe). Goering (Dora), Ztschr. f. Konstit. (Berl.), 1922, **8**, 312-335.

This is incidentally of endocrine interest since the influence of the glands of internal secretion (particularly the **thyroids, gonads, hypophysis** and **epiphysis**) on adipose tissue is discussed because it is a question whether this influence is direct or indirect through the nervous system. There is a review of the evidence for the existence of various vegetative centers, especially in the region of the floor of the third ventricle, which might influence fat metabolism. From a study of lipodystrophia progressiva, lipomatosis, adipositas, dolorosa, scleroderma, glossy skin, hemiatrophia and hemihypertrophia faciei the author concludes that various nerve centers and the sympathetic nervous system are intimately involved. In connection with clinical and experimental dystrophia adiposo-genitalis the conclusion is drawn that the fat regulating center is in the floor of the third ventricle. It is mostly based upon literature, 126 references being given.—A. T. R.

(ENDOCRINE) The new clinic. An advance movement in child welfare and race regeneration. Haberman (J. V.), Boston M. & S. J., 1920, **182**, 450-451.

The author points out, among other things, the desirability of a careful survey of the endocrine status of each child, with a view to early corrective procedures in case of defects.—R. G. H.

(ENDOCRINE) Sclérodermie partielle traitée avec succés par l'opothérapie associée. Hügel, Cong. d. Dermatol. et Syphil. de langue franç., 1922; abst., Presse méd. (Par.), 1922, **30**, 561.

A woman of 25 years was troubled with scleroderma in the foot and calf of leg which inconvenienced her considerably in walking and in her work. All other treatment having failed, the author prescribed extracts of **thyroid, ovary, hypophysis** and **adrenal.** In 15

days the lesions had almost disappeared and no longer interfered with her work. The author believes that in Alsace scleroderma is about equally frequent with **goiter.**—R. G. H.

(ENDOCRINE) Organotherapy in nervous conditions (Innersekretorische Therapie bei nervosen Zuständen). Laubenheimer, Klin. Wchnschr. (Berl.), 1922, **1**, 1329.

A short note. **Thyroid** is recommended for migraine. **Hypophysis** proved to be beneficial only once. **Parathyroid** and **ovary** are useless.—J. K.

Epileptiform manifestations in ENDOCRINOUS disorders. Leahy (S. R.), N. York State J. M. (N. Y.), 1922, **22**, 8-14.

There appeared to be a definite relation between deficient **ovarian** secretion and epileptiform attacks. There appeared to be a definite relation between **dyspituitarism** attended by deficient secretion and epileptiform attacks. Practically all of the cases showed more than one glandular involvement. Striking physical abnormality was absent, except in one case. The failure of the attack to disappear entirely in some cases may be due to the effect that glandular involvements other than those established were overlooked, and therefore not medicated, or establishment of the epileptic habits rendered this form of discharge of energy more difficult to control after being present for some time. Transitional forms of various endocrinous disturbances should be sought for in every case of epilepsy.—Arch. Diagn., 1922, **14**, 257-258.

Le syndrome ENDOCRINO-sympathique de la pelade (alopecia). Lévy-Frankel & Juster, Cong. d. Dermatol. et Syphil. de langue franç., 1922; abst., Presse méd. (Par.), 1922, **30**, 561.

Along with alopecia the authors always find endocrine disorders —**dysthyroidism, dysovarianism, frigidity, hypophysis** disorders, modifications of the oculo-cardiac, pilomotor and nasofacial reflexes, vasomotor troubles (dermagraphia, frailty of skin). These troubles and alopecia are favorably modified by organotherapy. The authors conclude that alopecio is due indirectly to the endocrine system.—R. G. H.

(ENDOCRINE) Syphilis. C. F. M. & C. L., Med. Sc. (Lond.), 1921, **3**, 229-301.

The article includes an excellent brief review of the current data on syphilis of the endocrine glands.—R. G. H.

(ENDOCRINOLOGY) The oculo-cardiac reflex (Dagnini-Aschner phenomenon)—its use in medicine and psychology. Naccarati (S.), Arch. Neurol. & Psychiat., 1921, **5**, 40-57; abst., Med. Sc. (Lond.), 1921, **4**, 150-151.

Naccarati gives a list of factors, both physiological and psychological, which influence the character of the response in normal subjects, and it becomes clear from his observations that the oculocardiac reflex has no diagnostic value whatever. It is unfortunate that he does not say this at once, and thus put in its proper perspective a phenomenon which has cumbered neurological literature unduly. Instead, he goes on to say that "it may constitute an index of the psychic condition and of the sympathetic-endocrine make-up of the subject, but only when other factors have been standardized. In normal persons the reflex index may serve as an indication of reflex control, moods, courage, emotions, etc., traits whose scales are wanting." All of which means precisely nothing. It seems characteristic of the craving for new and bizarre "signs," for ever fresh empirical diagnostic tricks, that it gives rise to an extensive and unscientific literature, which rises mushroom-like as each new phenomenon is recorded. The quotation given above from Naccarati's paper is typical of the scientific value and general style of the papers in which these new signs and wonders are proclaimed. The atrocious phrase "sympathetic-endocrine make-up" is an epitome of this class of neurological literature.—Abbreviated, R. G. H.

Referat über INNERE SEKRETION. Nakamura (H.), Verhandl. d. jap. path. Gesellsch. (Tokyo), 1916, **6**, Reprint 1-9.

An outline classification of endocrine disorders, illustrated with two excellent plates.—R. G. H.

(ENDOCRINE) New method of sterilization of organo-therapeutic products (Un nuovo metodo di sterilizzazione dei prodotti organoterapici). Paranhos (P.), Ann. d'ig. (Roma), 1921, **31**, 620.

By means of an isotonic solution of sodium fluoride, organotherapeutic products can be obtained containing 0.10 gm. of the given organ and 1 mgm. of NaF_2 to every cc. of the final product. Preparations of this sort remain indefinitely sterile and do not give rise to any trouble when injected into man.—Med. Sc., 1922, **6**, 233.

Histological changes in the ENDOCRINE organs after injections of ADRENIN and choline (Studi sul timo. II. Glandole endocrine e sangue nei polli iniettati con adrenalina e con colina). Pighini (G.), Riv. sper. di freniat. (Reggio-Emilia), 1921, **45**, 1-40.

Investigations of the histological changes occurring in various endocrine organs as the result of injections of adrenaline and choline. In the **thymus** adrenaline produced degenerative and choline hypotrophic effects.—Physiol. Abst., **7**, 257.

(ENDOCRINE) physiopathology of "vicious circle" after gastroenterostomy and its relation to high obstruction (La fisiopatologia del "circolo vizioso acuto" consecutivo alla gastroenterostemia

nei suoi rapporti colla occlusione alta). Razzaboni (G.), Arch. ital. di chir., 1921, **4**, 553; abst., Med. Sc., 1922, **6**, 201.

Intestinal occlusion was performed in dogs. The **adrenals** and **thyroid** showed evidence of toxic degeneration.—R. G. H.

Influence of the ENDOCRINE organs on morphogenesis (Weitere Untersuchungen über die Wirkung innersekretorischer Drüsensubstanzen auf die Morphogenie). Schulze (W.), Klin. Wchnschr. (Berl.), 1922, **1**, 895-896.

The author tried to remove completely the **thyroid** "anlagen" in 25 tadpoles of Rana fusca. He succeeded in only 6 animals; 4 of these were lost; the only two that were left grew rapidly, but metamorphosis began only when bovine thyroid was given. One tadpole without "thyroid-anlage" to which no thyroid was given has been living for over a year as a tadpole. In another series of experiments the author implanted in larvae of Bombinator pachypus thyroid of Bombinator pachypus, thyroid of the cow, normal human thyroid, thyroid of Graves' disease and **testicles.** The implantation of testicle had no effect. The implantation of thyroid caused a quickened metamorphosis with an arrest of growth. The influence of human and bovine thyroid was much more marked than was the thyroid of the same species. In some of the animals metamorphosis was so fast that they died. In one case, real prolapse of the brain was seen; this proves the great importance of endocrine secretions in the genesis of malformations.—J. K.

(ENDOCRINE) Maladie de Recklinghausen avec insuffisance polyglandulaire. Rœderer (J.), Réunion Dermatol. de Strasburg, May 14, 1922; abst., Presse méd. (Par.), 1922, **30**, 507.

A typical case is described of neuro- and dermo-fibromatosis with pigmentary lesions in a young girl of 19 years, whose mother also has pigmentary trouble. There is a hypoplastic **thyroid,** acroasphyxia and little resistance to fatigue. The author believes that endocrine factors play a more or less important rôle in the pathogenesis of this disease and proposes the use of extracts of thyroid, **ovary** and **hypophysis** in treatment.—R. G. H.

(ENDOCRINE) Syndrome polyglandulaire à symptomatologie complexe. Sainton & Peron (N.), III Réunion neurol. internat. ann., Paris, 1922; abst., Presse méd. (Par.), 1922, **30**, 615.

A man of 25 years, after having had meningitis at 10 months, continued to have optic atrophy and nystagmus. The patient showed adiposity, pseudogynecomastia, genital hyperplasia, and frigidity. He was tall in spite of marked kyphoscoliosis. The sinus was enormous, but the sella turcica was normal. There was also considerable thyromegaly and tremor. The biological **hypophyseal** tests were negative. This case brings up the question of the relation between

meningitic lesions of the base of the brain and the appearance of different symptoms of so-called hypophyseal syndromes.—R. G. H.

(ENDOCRINE) An analysis of ninety cases of functional disease in soldiers. Swan (J. M.), Arch. Int. Med. (Chicago), 1921, **28**, 586-602.

The ages, occupations, previous histories, particular complaints, symptomatology, pulse studies after exercise, blood pressures, etc., are all carefully recorded and tabulated. These are the cases variously diagnosed as irritable heart, effort syndrome, neurocirculatory asthenia, etc. Sixty-five per cent were recruited from sedentary occupations; 50 per cent gave a family history of nervous disease; no evidence of organic disease to explain the symptoms complained of could be found in any of them; 90 per cent gave evidence of previous or present subacute chronic infections. Some evidence of ductless gland disturbance was found in all of them. Removal of the foci of infection did not benefit the patients. Swan is strongly of the opinion that endocrine abnormality is the responsible factor. The treatment is very largely psychic. **Organotherapy** is not advised. —H. L.

(ENDOCRINE) Clinical interpretations of the basal metabolism test. Swanberg (H.), Illinois M. J., 1922, **42**, 39-41.

Attention is called to the importance of the correct interpretation of basal metabolism findings. Basal metabolism is increased in **thyroid** and **pituitary** hyperactivity, the leukemias, the fevers, late pregnancy, pernicious anemia, early **diabetes**, and cardiac decompensation. Basal metabolism is decreased in thyroid and pituitary hypoactivity, **Addison's disease**, extreme cachexia from tuberculosis, diabetes, starvation, and in some healthy persons running a slow pulse. A combination in a patient of two or more conditions characterized by opposing basal metabolism findings may in totality yield a plus or minus rate depending upon which disease plays the leading rôle in the patient. While in non-endocrine conditions (leukemia, diabetes, etc.) diagnosis can readily be made without basal metabolism observations, this laboratory procedure has become a necessity in diagnosis of diseases involving the thyroid and pituitary glands. Moreover, basal metabolism findings determine the severity of thyroid malfunction and indicate the treatment required.—I. B.

The etiological relation of the eye to the ENDOCRINE organs. Zentmayer (W.), Penn. M. J. (Harrisburg), 1922, **25**, 527-529.

Extirpation of the **thyroid** in dogs leads sometimes to porcelain-white corneal infiltration, blepharitis, lacrimation, conjunctivitis and partial blindness. Interstitial keratitis and bilaterial cataract have followed complete excision of the thyroid and **parathyroids**. The ocular complications of disease of the **pituitary** are regarded as produced by direct pressure and increased intracranial pressure.

However, glandular therapy has relieved amblyopia in undoubted **hypophyseal** disease. The ocular symptoms of hyperthyroidism, though very striking, are not constant and bear no relation to the gravity of the toxemia. The eye changes observed in **myxedema, cretinism** and **mongolian idiocy** are briefly mentioned. The possible bearing of endocrine disease on pigmentary degeneration of the retina and amaurotic family idiocy is commented upon.—H. L.

(GONADS) Experimental hyperfeminism (Ueber experimentellen Hyperfeminismus). Bondi (J.) & Neurath (R.), Wien. klin. Wchnschr., 1922, **35**, 520-522.

It is probable that the endocrine products of the mother during pregnancy have an influence on the child. This explains the fact that during the first days after birth the **mammary** glands of the child function slightly and that many new born girls bleed from the generative organs. To study this question experimentally the authors transplanted the **ovaries** of young rats in other female rats of the same age. The first remarkable effect was that out of 27 animals only 3 became pregnant. The grafts soon changed into cysts with a wall of connective tissue. Ovarian tissue very often could no longer be detected. It may be that the normal ovaries destroyed the transplanted ones. Each animal in which ovary had been transplanted had a very small infantile **uterus.** Though the normal ovaries contained **corpora lutea** the glands of the uterus were not at all developed, the submucosa also was poorly developed and the muscles were very thin. Perhaps the secretion of the normal and of the transplanted ovary neutralize each other; if this is true, one can believe that the ovary does not produce enough hormones to cause the development of the uterus, since the hormones are destroyed at once by the hormones of the graft.—J. K.

(GONADS) Experimental alteration of sex in the Triton alpestris (Changement expérimental du sexe chez le Triton alpestris). Champy (C.), Compt. rend. Soc. de biol. (Par.), 1921, **172**, 1204-1207.

Two male Tritons, reduced to a sexually neutral condition by starvation, and then well fed, took on the external characteristics of females. One was killed, and was found to have fatty bands, with scattered indifferent spermatogonia, in place of **testes.** The other was killed 3 months later, and was found to possess **ovaries** lying medially to the degenerated testes. This observation is contrary to the theories of the predetermination of sex.—Physiol. Abst.

(GONADS) Two cases of total genital infantilism (Deux cas d'infantilsme total de l'appareil génital). Chauvin & Vigne, Comité méd. d. Bouches-du-Rhone, 1922; abst., Presse méd. (Par.), 1922, **30**, 596.

Two women, normal in other respects, had infantile genitals. The ovaries were small and insufficient, the uterus of pubescent type, the vagina short and narrow and the vulva glabrous and infantile. The authors believe that it is very rare that these women have a normal general organic development.—R. G. H.

(GONADS) Use of lutein solution hypodermically for the control of nausea and vomiting of pregnancy. Coffey (T.), Am. J. Obst. & Gynec. (St. Louis), 1922, **3**, 513-516.

A clinical report of 62 selected cases in which this method was used, 88.6 per cent being improved. An average of six and a half injections per patient was given. The least number of injections was one and the highest was twenty-five. If the discomfort was severe, the injections were given daily, but usually they were given every other day. No control study of cases by other methods was apparently made.—E. N.

The INTERSTITIAL cells of the TESTICLE and the secondary sex characteristics in the fish (Glande interstitielle du testicule et caractères sexuels secondaries chez les poissons). Courrier (R.), Compt. rend. Soc. de biol. (Par.), 1921, **85**, 42-43.

In the male stickleback the secondary sexual characteristics appear at the middle of April. At this time the formation of spermatozoa has ceased, and the interstitial cells of the testis show indications of secretory activity.—Physiol. Abst.

(GONADS) Dystrophy adiposogenitalis and gerodermia in dementia precox (Syndrome adiposo-génital avec gérodermie chez un dément précoce). Demole, III Réunion neurol. internat. ann., Paris, 1922; abst., Presse méd. (Par.), 1922, **30**, 605.

Anatomical examination showed neither hypophyseal nor tuberous lesions, but important lesions of the interstitial cells of the testicles.—R. G. H.

(GONADS) On the relations between fertility and nutrition. I. The ovulation rhythm in the rat on a standard nutritional régime. Evans (H. M.) & Bishop (K. S.), J. Metab. Research (Morristown, N. J.), 1922, **1**, 319-327.

It is conceivable that certain nutritive régimes may permit growth to occur and yet may prevent or interfere with the cyclic ovulatory mechanism. Good general growth or weight maintenance signifies a satisfactory ovulatory mechanism, but not necessarily the ability to bear young. Ovulation, when compared with implantation and placental function, is a relatively hardy mechanism and much if not most sterility must be traced to uterine failure. The authors report the study of several series of rats from the standpoint of the influence upon the length of the oestrous cycle of a standard diet as

compared with a generous table scrap diet. The microscopic criteria determined by Lang and Evans for the detection of oestrus were adhered to, and the ovulation rhythm was observed for a period of about 50 days. In both series, from 74 to 80 per cent of the oestrous cycles observed in animals on either of the nutritive régimes were of the normal four or five days duration, the adequacy of the standard diet thus seeming assured. This diet consisted of wheat (whole ground), 67.5; casein, 15.0; whole milk powder, 10.0; sodium chloride, 1.0; calcium carbonate, 1.5; butterfat, 5.0.—E. N.

(GONADS) Hermaphroditism in a woman of 22 years, having feminine appearance and masculine characteristics (Hermaphrodisme chez une femme de vingt-deux ans ayant un état civil et un emploi masculins). Fourguet & Coquet, Soc. de méd. & de chir. de Bordeaux, 1922; abst., J. de méd. de Bordeaux, 1922, **94**, 282.

The patient began menstruating regularly at 14. The general appearance was feminine, but the clitoris was 4 cm. long and the vaginal orifice minute. No uterus could be palpated.—R. G. H.

(GONADS) The ovarian function. Graves (W. P.), Am. J. Obst. & Gynec. (St. Louis), 1922, **3**, 583-591.

Cessation of ovarian function, as a result of operation, radium or the natural menopause, produces cessation of menstruation, local atrophy of the external genitalia, and temporary vasomotor disturbance. Cessation of menstruation as a fact per se has no specific permanent effect on a woman's general organism. Abnormal postoperative atrophy of the external genitalia is a rare occurrence, and is no more frequent after hystero-oöphorectomy than after the natural menopause. Vasomotor disturbances occur in about 80 per cent of cases, with equal frequency after castration and radiation. There is no reason for the patient to fear the acquisition of abnormal fat when the operation has been performed after full maturity From such observations the author concludes that after constitutional maturity the chief province of the ovary is one of reproduction and that as an organ of internal secretion it is otherwise comparatively unimportant. Until the age of complete physical and mental maturity (on an average of 22 years), the ovaries are of great importance and should be sacredly preserved, both for their reproductive and secretory value. In the decade following full maturity the integrity of the ovaries should be carefully guarded, for this is the most important child-bearing epoch of the woman's life. During this decade conservation should be observed as far as possible, but if radicalism seems necessary for the patient's welfare, it may be practiced without fear of injury. Toward the latter part of the fourth decade, and even more after the age of 40, the importance of the ovary as an internal secretory gland becomes less and less until, by the age of 45, it need scarcely be regarded at all, except from a purely sentimental standpoint. Graves does not believe in

leaving the ovaries in situ in operations where the removal of the uterus is necessary.—E. N.

(GONADS) Genital organs of hermaphroditic fur seals. Hanna (G.), Am. Naturalist (N. Y.), 1921, **55**, 473-475.

Two cases of false hermaphroditism in the fur seal are reported. One was preponderatingly male and the other female. The endocrine significance is not discussed.—W. J. A.

GONADS and senility (Keimdrüsen und Alterszustand). Harms (W.), Fortschr. d. Naturwissensch. Forsch. (Berl. & Vienna), 1922, **77**, 189-298.

An excellent general review on this subject. Bouin, Ancel, Steinach and others have exaggerated the importance of the **interstitial cells.** They reported that sperm cells have no endocrine function. Plato, Kyrle, Stieve, etc., on the other hand, believed that the interstitial cells are only trophic elements for the sperm cells. Steinach has stated that a certain parallelism exists between the number of interstitial cells and the intensity of the secondary sexual characteristics and that autoplastically grafted **testicles** remain infantile, have no sperm cells and therefore show their endocrine function by the interstitial cells. This, however, has not been proved, as the grafted testicle contains many unripe spermatogones and Sertoli's cells to which the endocrine function may be attributed. The same is true with testicles transplanted in castrated female animals. Harms always found Sertoli's cells or cells derived from those in the graft. Some animals are without interstitial cells (testicle of the worms, **ovary** of amphibia and **Bidder's organ** in toads) and with secondary sexual characteristics. It is, however, quite possible that the interstitial cells have an endocrine function. The author often observed in histological pictures that interstitial cells gave substances to the capillaries. He believes that the endocrine substance of the testicle is made by degenerating or secreting spermatogones and Sertoli's cells, that it is kept in the interstitial cells in the form of a "Prosekret" and that in these cells this "Prosekret" is changed into the real "Sekret." In Bidder's organ, especially, many structures are found which sustain this theory.—J. K.

(GONADS) Artificial glycosuria and its importance in the early diagnosis of pregnancy (Über Künstlich erzengte Glykosurien und ihre Bewertung für die Frühdiagnose der Gravidtät in der Praxis). Hellmuth (K.), Klin. Wchnschr. (Berl.), 1922, **1**, 1152-1153.

The author compared 3 tests for pregnancy. According to the Frank-Nothmann test, when 100 gm. of glucose are given on an empty stomach to a pregnant woman, glucosuria without hyperglycemia occurs. According to the Kamnitzer-Joseph test the injection of 2-2.5 mg. of phloridzin on the empty stomach in pregnant women produces glycosuria. In the Roubitschek test 10 gm. of

glucose are given on the empty stomach. Twenty minutes later 0.5 cc. of a solution of suprarenal 1:1000 is injected and glucosuria without hyperglycemia is found in pregnancy. The Kamnitzer-Joseph and the Roubitschek test are of no value; the first one is often positive in women who are not pregnant and the second is never positive. The Frank-Nothmann test is rather reliable. Among 115 women who were not pregnant it was positive only 5 times.

—J. K.

(GONADS) Hormonal sterilization of female animals through subcutaneous transplantation of OVARIES of pregnant females (Ueber hormonale sterilisierung weiblicher Tiere durch subcutane Transplantation von Ovarien trächtiger Weibchen). Haberlandt (L.), Arch. f. d. ges. Physiol. (Berl.), 1922, **194**, 235-270.

Of 8 rabbits into which ovaries of pregnant rabbits had been transplanted subcutaneously 5 showed a varying sterilization of almost 3 months' duration, while 3 were not markedly affected. Of 8 guinea pigs 4 gave negative results, 3 showed a delayed conception of 3 to 4 weeks, and the eighth no conception after 10 months (perhaps due to other causes). In similar experiments the transplanted ovaries were examined histologically at varying periods of from 1 to 10 months. The greater part of the organ remained, especially the interstitial cells. (Two experiments each on rabbits and guinea pigs with **corpus luteum** optone injections gave negative results.) Haberlandt suggests that this method of inducing partial sterilization may have some subsequent application in practical medicine.—A. T. C.

(GONADS) Chlorosis and illustration of a case of male chlorosis (Betrachtungen über Chlorose im Anschlusz an die Demonstration eines lehrreichen Falles von viriler Chlorose). Holler (G.), Folia hæmatol. (Leipz.), 1922, **27**, 221-250.

Description of a boy of 17 with tuberculosis and typical chlorosis. The author believes that these two diseases are independent. He also states that in woman chlorosis is caused by dysfunction of the interstitial cells of the **ovary**. It is astonishing, therefore, that it is so rare in men, for one would expect that dysfunction of the interstitial cells of the **testicle** would produce male chlorosis. Perhaps very light cases of chlorosis are not rare, but are not recognized. It is also possible that the **eunuchoidism** before the onset of puberty in boys is equivalent to chlorosis in girls. Such boys often have sisters with chlorosis. The author concludes that the dysfunction of the "Pubertätsdrüse" is responsible for chlorosis in man as well as in woman.—J. K.

(TESTES) The Russian-Roumanian castrated sect of Skopzi (Uber die russisch-rumänische Kastratensekte der Skopzen).

Koch (W.), Veröff. a. d. Kriegs-u. Konstitutionspathol., 1921, **2**, 1-39.

See Endocrin., 1922, **6**, 410-411.—W. J. A.

(GONADS) Two cases of hermaphroditismus verus (Zwei Fälle von Hermaphroditismus verus). Kolmer (W.) & Scheminsky (F.), Arch. f. d. ges. Physiol. (Berl.), 1922, **194**, 362-364.

Egg cells have been found in the testis of a specimen of Esox lucius and also in a specimen of Salamandra maculosa.—A. T. C.

(GONADS) Function of the interstitial cells of the TESTICLE (Die Funktion der Zwischenzellen des Hodens). Jaffé (R.), München. med. Wchnschr., 1922, **69**, 873.

A short note. When spermatogenesis is disturbed the interstitial cells may increase or decrease in number. The interstitial cells have a trophic and a resorptive function, but they probably have an endocrine function also, correlating with the other endocrine functions of the body.—J. K.

(GONADS) Are there interstitial cells only in higher vertebrates (Finden sich Zwischenzellen nur bei den höheren Wirbeltieren)? Kolmer (W.) & Scheminsky (F.), Arch. f. d. ges. Physiol. (Berl.), 1922, **194**, 352-361.

Interstitial cells have been found definitely in the cyclostome Myxine, the holocephaloid Chimaera monstrosa, the elasmobranch Torpedo marmorata, and the teleosts Myrus and Esox lucius, and with great probability in Raja punctata and Cepola rubescens. In a number of other fishes the amount of material available was small; interstitial cells were not found and further experiments are being made. Taken in conjunction with Courrier's results (Endocrin., **6**, 338), these lead to the conclusion that at any rate at times male gonads of all vertebrates contain interstitial elements.—A. T. C.

(GONADS) A case of painful gynecomastia cured by radio-therapy (Un cas de gynécomastie douloureuse guérie par la radiothérapie). (Laederich & Le Goff, Bull. et mem. Soc. méd. des hôp. de Par., 1922, **46**, 764-767.

A man of 77 years who gave a history of acute blennorrhagia without orchitis at 20 years of age presented a bilateral mammary enlargement of a year's duration. The right gland was slightly more enlarged than the left and was some 12 cm. in diameter. The nipples were prominent and surrounded by pigmented areolar tissue. The skin was normal. The glands were firm like those of a pubescent maid and well lobulated. The testicles were normal on inspection and the patient was sexually potent. Radio-therapy was given on one side. A cold abscess of the breast developed on the untreated side. The breasts before treatment were excruciatingly painful.

Continued radio-therapy obliterated the pain and caused a diminution in the swelling.—F. S. H.

(GONADS) Women with penis. Loeser, Klin. Wchnschr. (Berl.), 1922, **1**, 1283.

From their 10th year two sisters showed development of a penis and a masculine distribution of hair. Pneumo-radiography of the abdomen disclosed probable hypertrophy of both **adrenals.** There were pathological changes in the sella turcica.—J. K.

(GONADS) Hermaphroditism as an endocrine disturbance (Hermaphroditismus als innersekretonische Störung). Loeser & Israel, Deutsche med. Wchnschr. (Berl.), 1922, **48**, 853.

Demonstration of two sisters with pseudohermaphroditism. The inner organs were female, as was seen after a laparotomy; the vagina was very small; each sister had a large penis but a female psyche. Pneumoradiography of the region of the kidneys showed enlarged adrenals.—J. K.

(GONADS) Steinach's operation versus rejuvenation (L'opération de Steinach peut-élle réaliser le rajeunissement de l'organisme animal)? Marinesco (G.), Presse méd. (Par.), 1922, **30**, 309-311.

Marinesco questions the applicability of the term "rejuvenation" to the results obtained by Steinach's ligation of the ejaculatory ducts and thinks that the cells of Leydig have no claim to the title of "puberty gland," although they doubtless secrete a specific hormone. His own experiments show the presence of a characteristic biochemical substance in the cells of Leydig, revealed by their staining reaction to benzidene and hydrogen peroxid (peroxidase reaction); whereas the oxidase reaction, produced by the use of dimethylparaphenilenediamin and alpha-napthol, only occurs in the reproductive cells, a fact which proves that a chemical difference between the two types of cells exists. He points out that senility, on the other hand, is a very complex process, which causes fundamental changes in the chemistry of all the tissues, and especially in the colloid constituents of all the body cells. Since it is known that both colloids and enzymes are subject to senescence; that the "ageing" of colloids, globulins, serum albumen, carbohydrates and lipoids is characterized by dehydration, degeneration and precipitation; and that the degeneration of albuminoids is an irreversible process, the mere retention of one or more hormones cannot be said to bring about rejuvenation. Marinesco discusses the changes wrought in three patients (a tabetic and two patients with Parkinson's disease) to prove that the results obtained were merely a transient improvement of the pathologic symptoms during two months and an equally transient revival of sexual activity, but that neither the ataxia of the tabetic, nor the Parkinsonian symptoms were permanently relieved. Temporary reactivation of certain physiologic functions should not be described

as "rejuvenation," which would require profound, complete and unattainable changes in the entire organism.—G. L.

(GONADS) Dysgenitalism in two brothers (Dys-genitalismus bei two Brüdern). Mayer (C.), Klin. Wchnschr. (Berl.), 1922, **1**, 244.

See Endocrin., 1922, **6**, 435.—J. K.

Vitreous hemorrhage at MENSTRUATION. Meanor (W. C.), Penn. M. J. (Harrisburg), 1922, **25**, 494.

Case report of a married woman, aged 33, in whom hemorrhage into the vitreous humor occurs at every menstrual period. The hemorrhage usually begins on the second day of menstruation. The vitreous becomes so cloudy that the fundus cannot be seen, but clears up before the next period. The patient has had blurred vision during her periods ever since menstruation began. She is the mother of two children and had the hemorrhage every month during her pregnancies. There has been no epistaxis.—H. L.

(GONADS) The importance of the lipoids in the human OVARY Ueber die Bedeutung der Ovariallipoide). von Mikulicz-Radecki (F.), München. med. Wchnschr., 1922, **69**, 851-854.

In cells which function and which are in a state of development (egg cells, granulosa cells, theca cells in the follicles and lutein cells of the gravid **corpus luteum**) cerebrosides, phosphatides and other complicated lipoids are found. When these cells begin to lose their function (e. g., thecal lutein cells in an atretic corpus) neutral fats are found in them and the lipoids gradually disappear. The last remains of such cells are masses of neutral fats, fatty acids and soaps. The author believes that the lipoids are endocrine products formed by the lutein cells immediately before fecundation and during the first of **pregnancy**. The experimental work of Iscovesco, Fellner, Herrmann, etc., have proved that it is possible to extract from the ovary complicated lipoids which, when injected, produce symptoms closely resembling those of beginning pregnancy.—J. K.

(GONADS) A study of testis and ovary grafts on the hen's egg and their effects on the embryo. Minoura (T.), J. Exper. Zoöl. (Phila.), 1921, **33**, 1-63.

A study of nearly 600 eggs in which grafts of testis or ovary were made on the chorio-allantoic membrane. Modifications of the reproductive organs of the hosts took place, giving forms that were intermediate between the male and female. The sizes of gonads and the persistence of the Mullerian ducts were considerd particularly. The author concludes that the differentiation of one sex is stimulated by the presence of a graft of the gonad of the same sex and inhibited by a graft of the opposite sex.—M. M. H.

On the physiological properties of the GONADS as controllers of somatic and psychical characteristics. IV. Gonad transplantation in the guinea pig. Moore (C. R.), J. Exper. Zoöl. (Phila.), 1921, **33**, 365-391.

A study of over 50 guinea pigs of both sexes which have undergone complete castration at the age of 10 to 20 days. Gonads from animals of the opposite sex were implanted in these castrated individuals, repeated grafts being made in many cases. The presence of ovarian grafts in the male led to hypertrophy of the teats, while a graft of testicle in the female caused a pronounced modification of the clitoris towards the male condition. The psychical characteristics of the females were so modified that the animals behaved like males; but the reverse effect was not observed in the males, which retained their normal psychical characters.—M. M. H.

(GONADS) Interstitial cells and dementia praecox. I. Mott (F. W.) & Such (M. P. y), II. Such (M. P. y), Proc. Roy. Soc. Med. (Lond.), 1922, **15**, 1-14; 14-30.

Fully illustrated articles on the morbid histology of the testis. Changes in the reproductive organs form "a part of a generalized defect of durability and vital energy in the whole body most manifest in the brain, especially the cortex and the reproductive organs."

—Physiol. Abst., **7**, 130.

(GONADS) Changes in the interstitial tissue of the TESTICLE in consequence of deficiency in water-soluble accessory substance B (Sulle modificazioni del tessuto interstiziale in seguito a deficienza di vitamina B nella dieta). Novaro (P.), Boll. d. Accad. med. di Genova, 1920; abst., Pathologica, 1920, **12**, 405.

The testicles of four young pigeons, kept for two months on a diet of polished rice, were examined histologically. Material was fixed partly in Zenker and partly in Flemming. The testicular tubules were found atrophic, and their epithelium degenerated in many places. The intertubular spaces were larger than in normal specimens and filled with interstitial cells. These, instead of appearing isolated or in small groups of two or three, were arranged in well delimited rows supported by flattened connective tissue elements. The interstitial cells had increased, not only in number, but also in size, their nuclei being also larger than those of normal cells. In the specimens fixed in Flemming's fluid the cytoplasm of such cells appeared filled with many granules stained deeply black. The author comes to the conclusion that deficiency of the water-soluble accessory food factor B, causes a true hypertrophy and hyperplasia of the so-called interstitial gland of the testicle.

—Med. Sc., 1921, **4**, 168.

(GONADS) The physiology of the TESTIS (Contribución experimental para el studio de la fisiologia del testiculo. Segundo

memoria). Ocaranza (F.), Rev. Mex. de biol. (Mexico), 1922, **2**, 219-235.

This is a continuation of the work on guinea pigs reported a year ago (Rev. Mex. de biol., 1921, **1**, No. 6) and deals with the effect of castration and testicular grafting on the number of blood corpuscles per unit volume of blood. The previous report was based on 4 complete and 3 incomplete castrations from which the author made the tentative deduction that the blood changes which resulted might be due to some general metabolic disturbance produced by the absence of some testicular autacoid that influences the hemopoietic organs. The number of additional animals studied is not stated, but there is given the protocol of 6 individuals for a period of several days before double castration to about a month after. These experiments, like the previous ones, showed a constant decrease of various degrees in both red and white corpuscles just after castration, followed by an increase frequently to above normal and then waves of alternate decrease and increase—the rise in the white count coming a little ahead of the corresponding increase in the red. The leucocytosis is largely due to neutrophiles with a tendency towards lymphocytic adjustment. Since eosinophilia was observed in only 2 cases to follow immediately after the operation and in one case 15 days after, and since the changes in the blood count occur in waves, the author is now inclined to think that the variation is not due to general metabolic disturbances, but rather that some organs are constantly connected with blood formation and others are only occasionally thus involved. In the absence of the former the corpuscles decrease to a limit compatible with physiological equilibrium and then the latter organs begin to influence blood formation, whereupon the bone marrow becomes stimulated to increased hemopoietic function. The variations in the blood count and in the behavior of the animals produced by grafting testicular tissue into both castrated and non-castrated males and into pregnant females are recorded in 10 cases. The results were variable so that no particular conclusions are drawn. The author realizes that a disturbing factor might be the rapid absorption of the grafted tissue which might act as foreign protein. He noted, as others have done, that castrated animals with iso- or homo-grafts retained the sexual instincts. Some became more than usually aggressive after absorption of the graft. Testicular grafts did not change the maternal instincts of non-castrated females. The grafts, one month after implantation, showed an almost complete disappearance of the interstitial ("diastemática") gland. The germinal epithelium in each tubule formed a floculent colloidal complex in the center of which were remains of nuclei and spermatozoa. Grafts from which the tunica albuginea had previously been removed were enveloped in a delicate connective tissue capsule similar in appearance to the original tunica albuginea. Fourteen references are given.—A. T. R.

(GONADS) Hen feathering in cocks. Pease (M. S.), Proc. Cambridge Phil. Soc., 1922, **2**, 22-26.

Morgan attributes suppression of cock-feathering in hens and in cocks with hen-feathering to the presence of **luteal cells** in the generative organs. The author finds these cells present in all cocks except when spermatogenesis is in full swing. The cells form most likely a food supply for sperm formation, and were absent from the 2 birds (on which Morgan apparently bases his theory) he examined, because spermatogenesis was inactive.—Physiol. Abst., **7**, 262.

The so-called INTERSTITIAL tissue in the testis of the urodele batrachian (Sur un prétendu tissu interstitiel dans le testicule des batraciens urodèles). Pérez (C.), Compt. rend. Acad. d. Sc. (Par.), 1921, **172**, 1443-1445.

The tissue in the testis of Triton, described as interstitial by Champy, has nothing in common with the interstitial cells of the mammalian testis. It is due to phagocytic changes in the testicular tissue proper.—Physiol. Abst., **6**, 327.

(GONADS) Numerical law of regression of certain secondary sex characters. Pézard (A.), J. Gen. Physiol., 1921, **3**, 271-283.

Postpubertal castration is followed in cocks by a regression of the comb. In a few weeks the aspect and dimensions of this organ is similar to that of cocks castrated before puberty. Eight animals were used.—H. A. McC.

(GONADS) Epilepsie et fonctions OVARIENNES. Rebattu, Mollon & Sédaillan, Bull. Soc. méd. d. hôp. đe Lyon, 1922; abst., Presse méd. (Par.), 1922, **30**, 620.

The authors have studied the reports on a number of patients in the hospital at Perron on the relation between epilepsy and the genital life in a woman. They studied the influence of the establishment of menstruation on the first crises, the influence of the first menstruation on the crises existing previously, the coincidence of the crises and the menstrual periods, the influence of the cessation of menstruation on account of pregnancy, castration and the menopause, and the results of ovarian organotherapy. They concluded, in spite of the complete failure of ovarian medication, that in about a third of the cases there was a slight relation between epilepsy and functions of the ovary. The menopause often leads to disappearance of the crises or diminution of their frequency, but the first crises sometimes appear at the menopause. In this case, the relation between epilepsy and the genital functions remains through life. In 3 patients the first crises appeared at puberty, causing their menstrual periods to come to an end, as in the menopause. Other endocrine troubles, such as disorders of **adrenal, hypophysis or thyroid** origin are not involved. The internal secretion of the ovary seems to be

the only one which plays a rôle in epilepsy, and, moreover, this is inconstant.—R. G. H.

(GONADS) Primary sterility: A study based on 400 cases. Rongy (A.), Am. J. Obst. & Gynec. (St. Louis), 1922, **3**, 553-556.

The various causes of sterility are discussed, the author warning against the "blind acceptance of the theory that the organs of internal secretion are responsible for sterility." The treatment of sterility consists chiefly in being able to select the patients who are likely to respond to treatment. Those patients with congenitally defective organs should be left alone.—E. N.

TESTICLE transplantation (Hodenüberpflanzung). Rosenthal, München. med. Wchnschr., 1922, **69**, 137.

See Endocrin., 1922, **6**, 457.—J. K.

(GONADS) A special type of atresia of the graafian follicles of the rabbit as revealed by the tanno-ferric method [Sur une forme particulière d'atrésie des follicules de De-Graaf (lapine), révélée par la méthode tanno-ferrique]. Salazar (A. L.), Am. J. Anat. (Phila.), 1922, **30**, 503-523.

This special type of atresia is to be observed in the small follicles of the ovary of ovigenic type, and is characterized by the formation in the interstices of the cells of the granulosa of a long tannophilic cord. The author examines the connection of this type of atresia with hydropic atresia in the ovigenic cords and its remains (epithelial nodules, anova follicles of Regaud), recently described by him, and discusses the significance of the cases described.

—Abst., Wistar Institute.

(GONADS) Convulsive and anticonvulsive action of the genital hormones (Azione convulsivante ed anticonvulsivante degli ormoni genitali). Sanchirico (F.), Folia med. (Napoli), 1922, **8**, 161-167.

Epilepsy is said to be due in many cases to the action of hormones in the nervous system. This is indicated indirectly, according to Sanchirico, by the resemblance between the convulsions produced by hormones (especially genital) and those caused by strychnia. The data, however, are equivocal. The author injected into rabbits gonad extracts sufficient to produce convulsions and studied the influence of the dosage factor. Usually positive results were obtained.—P. M. N.

(GONADS) Modern experimental sexual research, especially the recent experiments of Steinach ("rejuvenescence") [Moderne experimentelle Sexualforschung besonders die letzten Versuche Steinachs ("Verjüngung")]. Sand (K.), Ztschr. f. Sexualwissensch. (Berl.), 1920, **7**, 177-197.

An exceptionally lucid and well organized review and discussion of the subject with considerable emphasis upon the work of Steinach and similar experiments, upon which Sand is well qualified to speak, having for several years been engaged in similar investigations.
—A. T. R.

Changes in the vaginal epithelium of the guinea pig during the OESTROUS CYCLE. Selle (R.), Am. J. Anat. (Phila.), 1922, **30**, 429-449.

A syringe method for taking vaginal samples is given as being more satisfactory than any other method yet used. Its use in testing the cellular contents of the vagina during the various stages of the oestrous cycle of the guinea pig is described. The length of the oestrous cycle for this animal was found to overage 15.87 days, which corresponds closely to the determination of Stockard and Papanicolau. Four well-defined periods or stages, in addition to the interval, are recognized for the complete cycle.—W. J. A.

(GONADS) Modification of the indications for operative interference in gynecology imposed by present radium therapy. Skeel (R.), Northwest Med. (Seattle), 1922, **21**, 131-136.

Menorrhagia, especially the menstrual hemorrhages of the adolescent period, are probably often due to endocrine disease, more particularly **ovarian** instability or overactivity. Radical surgery should be abandoned in these cases. Radium in doses that will temporarily stop menstruation is the treatment of choice. The remainder of the article though excellent is not of endocrine interest.
—H. L.

Influence of injections of foetal, placental and uterine extracts on the gravid CORPORA LUTEA in the hysterectomized guinea pig (Influenza delle iniezioni di estratti fetali, placentari, uterini sui corpi lutei gravidici di cavie isteroctomizzate). Verdozzi (C.) & Cavalieri (R.), Arch. di fisiol. (Firenze), 1920, **18**, 1-13.

Subcutaneous injections of aqueous extracts of guinea pig embyros into guinea pigs on which hysterectomy had been performed during the first half of pregnancy present, up to a point, the rapid involution which the corpora lutea undergo when hysterectomy only is performed. Under the same experimental conditions, injections of placental and uterine extracts have no effect of the sort. This appears to support Verdozzi's opinion that the persistence of the corpus luteum during pregnancy is, at least in part, due to "chemomorphotic" substances passing through the placenta from the embryo to the mother.—Physiol. Abst.

(GONADS) Influence of x-rays on the sex glands (Über Geschlechtsbeeinflussung durch Röntgenstrahlen). Weiloch (J.), Strahlentherapie (Berl. u. Wien.), 1921, **13**, 114-125.

Experiments on animals and statistics from men show that an influence on sex by irradiating the sex-glands with x-rays does not exist.—Physiol. Abst., **7**, 131.

Structures and homologies of free-martin GONADS. Willier (B. H.), J. Exper. Zoöl. (Phila.), 1921, **33**, 63-129.

Free-martin gonads show three degrees of transformation in the male direction. These transformations involve the sexual cords, interstitial cells, rete, epididymis, and the distribution of the blood vessels. The transformed gonad may be a morphologically complete **testis**, but spermatozoa are never formed. Although hypertrophy of interstitial cells may occur it is here independent of atrophy of the male germ cells, and does not influence secondary sexual characters or instincts.—M. M. H.

(GONADS) Phlorizin glycosuria and the diagnosis of pregnancy (Phloridzinglykorurie und Schwangerschaftsdiagnose). Zondek (B.), Zentralbl. f. Gynäk. (Leipz.), 1922, **46**, 851-853.

If, after injection of 2 mg. of phlorizin no glycosuria is seen, it is highly probable that the patient is not pregnant.—J. K.

La pituitrina. Barbabosa (A. V.), Observador Med., 1920, **2**, 326-332.

A general discussion of the pharmacology of pituitrin with special reference to the **uterus**.—R. G. H.

Technique, résultats et indications de la radiothérapie dans les tumeurs de la région HYPOPHYSAIRE. Béclère, III Réunion neurol. internat., Paris, 1922; abst., Presse méd. (Par.), 1922, **30**, 616.

Practically for the first time in 1907 radiotherapy was used for buccal irradiation. Gramegna had excellent success with this method. The frontal, parietal or temporal route can be used. There was already developed deep radiotherapy, and modern methods have improved its technique. There is now a way of indicating precise dosage, depth of irradiation and intensity of depth. The first two patients treated by Béclère were entirely cured. Since then 40 observations of hypophyseal tumors treated by radiotherapy have been reported by the author. The results were remarkable and included all the symptoms. There was improvement of vision and enlargement of the visual field (even after cessation of treatment), improvement of troubles due to intracranial hypertension, loss of excessive adipose tissue, reappearance of menstruation, arrest of development of osseous lesions in acromegaly, etc. Comparing the results of radiotherapy with other therapy, opotherapy or surgery, Béclère concludes that it is the treatment of choice for hypophyseal tumors, particularly in cases of **acromegaly** and **gigantism**, with the

exception of tumors of syphilitic origin and of syndromes of glandular deficiency.—R. G. H.

The action of the different extracts of the posterior lobe of the HYPOPHYSIS in the dog (Action des différents extraits de lobe postérieur d'hypophyse sur le chien). Béco, III Réunion neurol. internat. ann., Paris, 1922; abst., Presse méd. (Par.), 1922, **30**, 605.

Contrary to the opinion of certain physiologists, hypophysis extract undoubtedly causes oligiria, and also cardiotoxic action. Thus the endocrine secretions of the hypophysis play a rôle in the preservation of the vascular tonus.—R. G. H.

Ueber die HYPOPHYSIS. Biedl. München. med. Wchnschr., 1922, **69**, 796; Klin. Wchnschr. (Berl.), 1922, **1**, 1280.

The old fashioned idea of the anatomy of the pars anterior and the pars posterior is not right. The pars intermedia, which is very small in man, is a specific tissue; another specific part of the hypophysis is the pars tuberalis, that is, the tissue of the hypophyseal stalk. The pars anterior and the additional glands find their origin in the roof of the throat (Rachendach); the rest of the pituitary is of ectodermal origin. The pars anterior is an endocrine organ and its secretion is in the form of lipoids and granula (basophil or eosinophil). It contains a lipoid, the tethelin. The active principle of pars posterior and intermedia are histamin-like substances. Removal of the gland may produce cachexia. Tumors of the pars anterior, causing an increased function, produce **gigantism** and **acromegaly**. The changes in metabolism, which are seen in these diseases, are due to changes in the pars intermedia. **Dystrophia adiposogenitalis** and **diabetes insipidus** may be caused by disease of the base of the brain as well as by a disease of the pars intermedia. There is still another disease, very little known, having its origin in the same part of the basis of the brain. Its symptoms are atresia ani, polydactylism, retinitis, albuminuria, dullness, adiposity and characteristic disturbances of growth.—J. K.

HYPOPHYSEAL syndromes (Les syndromes hypophysaires). Anatomie et physiologie pathologiques, Camus (J.); Étude anatomopathologique, Roussy (M. G.), III Réunion neurol. internat. ann., Paris, 1922; abst., Presse méd. (Par.), 1922, **30**, 604-605.

A summary, largely of original work, on the problem. See Endocrin., **4**, 507-522. Extensive discussion is reported.—R. G. H.

Tumeurs de L'HYPOPHYSE et troubles visuels. Symptomes. Radiotherapie. Carlotti, Ann. d'ocul., 1922; abst., Arch. méd. belges (Brux.), 1922, **75**, 228.

Carlotti reports 4 cases of the hypophysis syndrome accompanied by visual disorders, after having studied the question from

the point of view of semeiology and treatment. The chiasmatic syndrome with **acromegaly** or dystrophia adiposogenitalis is due to a lesion of the hypophysis, appearing often in old syphilitics—twice among the 4 observations. From the point of view of early diagnosis it is necessary thoroughly to study the visual field. If the Wassermann test is positive treatment may be tried, but the case is usually hopeless. As soon as possible the patient should be treated with x-rays, giving him the maximum tolerable dose. If this does not appreciably affect the visual field at the end of a month the patient should be referred to a surgeon. Organic treatment (extracts of **ovary, thyroid,** and **hypophysis**) may have a generally good influence.—R. G. H.

(HYPOPHYSIS) Tumeur du 3e ventricule avec polyurie. Chabrol & Gambillard, III Réunion neurol. internat. ann., Paris, 1922; abst., Presse méd. (Par.), 1922, **30,** 615.

A case is reported of a tumor of the hypophysis which encompassed the chiasm, reached the tuber cinereum and encircled the pituitary stalk.—R. G. H.

Surgcal treatment of HYPOPHYSEAL tumors (Le traitement chirurgical des tumeurs hypophysaires). Cushing (H.), III Réunion neurol. internat. ann., Paris, 1922; abst., Presse méd. (Par.), 1922, **30,** 615-616.

This report, based upon 500 clinical observations of hypophyseal syndromes, takes no account of anything except verified tumors. They represent 60% of the cases operated upon (210). In comparison with other intracranial tumors (780) they represent 20% of the cerebral tumors. They are divided into 3 large groups: pituitary adenomas, 154 cases; congenital tumors (pharyngeal sac), 35 cases; suprasellar tumors that are not hypophyseal, 20 cases. In the clinic visual troubles are prominent manifestations; the opthalmoscope, the perimeter and radiography are used in their examination. By far the most important is the information furnished by the perimeter. Successive records show the progresson of the syndrome, and, above all, constitute the best criterion of the degree and the persistence of operative amelioration. From the surgical point of view it is possible to divide the tumors of the hypophysis into two groups—the suprasellar, which are preferably treated by an intracranial operation, and the infrasellar, whch may be approached through the nose (transphenoidal route). It is necessary to consider the immediate danger of the operation, and the degree and duration of amelioration which is to be expected. Two hundred forty-three operations have been performed with a mortality of 10%, including the cases in which extirpation could not have been successful—giving in reality a mortality of 5%. Operation by the transphenoidal route necessitates an incision at the level of the liga-

ment of the upper lip, the separation of the mucosa and of the septum, and ablation of a part of the septum and of the wall of the sphenoidal cells. A double speculum permits the carrying on of the rest of the operation under the control of sight. Of 154 cases of hypophyseal adenoma operated upon in this way, with more or less radical extirpation, marked amelioration followed in 50%, always with an enlargement of the visual field to the normal, amelioration with retardation of the malady occurred in 20% of the cases, and 20% already blind were not affected. The mortality was 8%. Operation by the transfrontal route involves a direct approach to the region of the chiasm by retraction of one of the frontal lobes. This is the preferable operation in all cases of suprasellar tumor; if the tumor is small it can be extirpated completely without wounding the chiasm thus affording permanent cure. Eleven of 27 cases of tumors of the pharyngeal sac operated upon in this way resulted favorably after the extirpation of cystic tumors. In 11 other cases the cyst was simply punctured and emptied and the period of amelioration was of short duration. In 5 cases the tumor was inoperable. Simple adenoma with excavated sella turcica can be extirpated by an operation by the lower route without great risk, and with hope of an immediate and lasting improvement of vision. Tumors of the pharyngeal sac should be attacked by the higher route, by osteoplastic craniotomy. Permanent cure can be expected only when the tumor has been extirpated. A remarkable series of projections illustrated the operative procedure and the history of a certain number of the cases.—R. G. H.

Adénome basophile du lobe antérieur de L'HYPOPHYSE avec adiposité. Demole, III Réunion neurol. internat. ann., Paris, 1922; abst., Presse méd. (Par.), 1922, **30**, 605.

Demole invokes the rôle of compression of adenoma on the infundibular region to explain the development of adiposity.

—R. G. H.

Treatment of HYPOPHYSIS tumors (Zur Behandlung der Hypophysentumoren). Denker, Verhandl. d. Gesellsch. deutsch. Nasen-, Hals- und Ohrenarzte, 1921; abst., Schweiz. med. Wchnschr. (Basel), 1922, **52**, 549.

The author describes a premaxillary approach to the hypophysis and reports three cases of tumors with bitemporal hemianopsia or blindness and other characteristic outstanding features. He undertook to bring about calcification by the injection of calcium lactate and Pregel's solution. Improvement followed in all three cases.

—R. G. H.

(HYPOPHYSIS) Tethelin—the alleged growth-controlling substance of the anterior lobe of the PITUITARY gland. Drummond (J. C.) & Cannan (R. K.), Biochem. J. (Lond.), 1922, **14**, 53-59.

An attempt was made to isolate tethelin according to the method of Robertson. The product obtained did not show the constancy in nitrogen and phosphorus content of Robertson's preparation nor was it white. In spite of these facts the conclusion is made that the substance "Tethelin" is a very impure mixture of lipoids. After severely criticising the statistical methods used by Robertson in his study of the effect of tethelin on the growth of mice the authors proceed to make a similar study of the effect of the impure mixture they prepared. Negative results were obtained, and the conclusion is drawn that the oral administration of anterior lobe of the pituitary gland is without influence upon the growth of mice.—F. S. H.

Tumeur HYPOPHYSAIRE d'origine hérédo-syphilitique. Syndrome thyro-testiculare consécutif. Herpès labial récidivant. Faure-Beaulieu & Georges, III Réunion neurol. internat. ann., Paris, 1922; abst., Presse méd. (Par.), 1922, **30**, 615.

The authors report a case of **myxodematous** facies, of glabrous skin, with testicular atrophy and frigidity. There was also anterior hypophyseal disorder, characterized by blindness, bitemporal hemianopsia and an enlargement of the sella turcica. The patient was a heredosyphilitic.—R. G. H.

Extrait HYPOPHYSAIRE et diurèse. Foix & Thévenard, III Réunion neurol. internat. ann., Paris, 1922; abst., Presse méd. (Par.), 1922, **30**, 616.

Hypophyseal extract had in 4 cases of tuberculosis manifest oliguric action; in one case it was without action and in another it produced slight increase in diuresis.—R. G. H.

(HYPOPHYSIS) Progressive muscular dystrophy. Friedman (E. D.), J. Nerv. & Ment. Dis. (N. Y.), 1921, **54**, 294-297.

A case of a boy of 16, with distinct muscular dystrophy, and showing some **pituitary** involvement, gave normal blood sugar content, attributed to the fact that the patient was still active.

—Chem. Abst., **16**, 744.

Les syndromes HYPOPHYSAIRES. Études clinique et thérapeutique. Froment (M. J.), III Réunion neurol. internat. ann., Paris, 1922; abst., Presse méd. (Par.), 1922, **30**, 606-607.

A summary of the present status of the problem; not amenable to abstracting. Extensive discussion is reported.—R. G. H.

La thérapeutique des syndromes HYPOPHYSAIRES. Froment (J.), III Réunion neurol. internat. ann., Paris, 1922; abst. Presse méd. (Par.), 1922, **30**, 616.

Radiotherapy is of equal importance with surgical treatment. Since the work of Gramegna and above all of Béclère it has given

remarkable results in the treatment of tumors of the hypophysis. As regards opotherapy, hypophyseal extracts should not be considered as equivalent to products secreted by the hypophysis. Two modes of action can be distinguished, namely, opotherapeutic and toxico-dynamic, but it is very difficult at present to indicate what results from the one or the other. We do not definitely know whether the histamine, discovered by the chemists, in the extracts used in therapeutics exists in the fresh gland. Different extracts used in the clinic vary greatly in their activity. We are still ignorant of the posology of these products. There is only one syndrome in which injections of extract of the posterior lobe have had a marked effect, namely, **diabetes insipidus**; but it seems to have a palliative rather than a curative action. When administered by mouth it is very much less active, due to the destructive action of digestive juices, especially the **pancreatic.** Its efficacy is increased when it is injected intraspinally. Some encouraging results, but rarely a complete cure, have been obtained in **infantilism** and **dystrophia adiposogenitalis.** There is increase in stature, growth of hair, reappearance of menstruation and sexual instincts and sometimes with extract of the anterior lobe even a loss of 25-50 pounds in weight. In **acromegaly** and **gigantism** organotherapy seems to be contra-indicated, but it is not always fatal.—R. G. H.

The regulation of the use of sublimate and HYPOPHYSEAL preparations by mid-wives (De la réglementation de l'emploi par les sage-femmes du sublimé et des extraits hypophysaires). Fruinsholz, Remy & Job. Bull. Soc. d'obst. et de gynéc. de Par., 1922, **11,** 36-38.

A discussion favoring limitation of use of hypophyseal preparations to physicians.—F. S. H.

(HYPOPHYSIS) Two cases of pituitary tumor with acromegalic syndrome cured by x-rays (Due casi di tumore dell' ipofisi con sindrome acromegalica curati coi raggi X). Gavazzeni (S.), Radiol. med. (Torino), 1920, **7,** 222.

One case had the complete clinical picture of acromegaly, and radiographically showed evidence of pituitary tumor. The symptoms of disease were of four years' standing, but the condition improved very much under x-ray treatment. The other case showed the same symptoms and signs in a milder degree, and the results of radiotherapy were equally good.—Med. Sc., 1921, **3,** 476.

Secretory activity of anterior lobe of HYPOPHYSIS during pregnancy (Sull' attivita secretiva della preipofisi in gravidenza). Gentili (A.), Sperimentale Arch. di biol. (Firenze), 1920, **74,** 286.

In large part a confirmation of known facts. The pars anterior progressively increases in cows from the beginning to the end

of pregnancy. The weight of the hypophysis in multiparous cows is 135 to 140 mgm.; at the beginning of pregnancy, 170 mgm., at the end, 350 mgm. In multiparous cows it may weigh 460 mgm. In these animals the pars anterior is excellent material for the "gravidic" cells, whose function is to secrete lipoid substances, possibly phosphatids. During pregnancy also the chromophobe cells appear to secrete great amounts of colloid.—Physiol. Abst.

DIABETE insipide et opothérapie HYPOPHYSAIRE. Gilbert (A.), Villaret (M.) & Saint-Girons (F.), III Réunion neurol. internat., ann., Paris, 1922; abst., Presse méd. (Par.), 1922, **30**, 616.

A case is described of an Italian of 31 years who, 2 years after having hemiplegia of syphilitic origin, began to be troubled with typical diabetes insipidus, with marked obesity. Daily, subcutaneous injections of posterior lobe of the hypophysis reduced the diuresis to normal and produced a loss of 2 kg. in weight. But this therapy gave no results after specific treatment had ended, and was without effect on the polyuria as well as the hemiplegia and obesity. The authors believe that the diabetes insipidus was not of nervous, but of hypophyseal origin; they based their view on the remarkable efficacy of the organotherapy, the absence of effect on polyuria of rachicentesis and the non-existence of clinical or biological signs of a nervous infundibular lesion.—R. G. H.

(HYPOPHYSIS) The pigmentary effector system. I. Reaction of frog's melanophores to pituitary extracts. Hogben (L. T.) & Winton (F. R.), Proc. Roy. Soc., 1922, **93**, 318-329.

The posterior lobe of the pituitary contains a specific stimulant which, if injected into the frog, brings about general and complete expansion of the dermal melanophores; a dose equivalent to 1.0003 to 0.0005 cc. of commercial "infundibular" preparations is sufficient to induce a darkening of the skin visible to the naked eye. This stimulant is not destroyed by pepsin or boiling; it is not identical with histamine, since neither histamine nor putrid meat extracts give this reaction. It is rapidly destroyed by trypsin. It is not rapidly destroyed by acid hydrolysis (continuous boiling with 0.5% HCl); and in this respect agrees with the oxytocic (uterine) and differs from the pressor principle. After cocaine, curare, atropine, and apocodeine it still evokes its characteristic response, and therefore acts probably directly upon the melanophores. The result of the experiments confirms the endocrine significance of the condition of general pigmental contraction found by Allen and others to follow removal of the pituitary gland in tadpoles. If Spaeth's observations are correct, the melanophores of amphibia and fish respond in an opposite manner to the pituitary autocoid; the action of the latter is also opposite to that of adrenaline in the amphibia.

—Physiol. Abst., **7**, 260.

HYPOPHYSIS and THYROID in carcinoma (Ueber Hypophyse und Thyreoidea bei Krebskranken). Karlefors (J.), Ztschr. f. Krebsforsch. (Jena), 1920, **17**, 195-235. 4 plates.

This work is based upon post-mortem material in Stockholm and involves a study not only of cases of carcinoma, but also of sarcoma, and of various other pathologic conditions in patients in the corresponding age periods. No change in the weight of the hypophysis was found in patients with carcinoma. Histologically, there was a notable decrease in the eosinophile cells with an increase in the chief cells, the basophiles remaining unchanged in numbers. In a few cases of chronic carcinoma there was an increase in the size of the nuclei of the chief cells. These changes were not, however, found to be specific for carcinoma, for similar changes were found in other patients, but much less frequently. In 4 out of 6 cases of sarcoma alterations of like character were observed. The changes described were more pronounced in advanced stages of carcinoma than in the earlier stages. Hence the author believes that the changes in the hypophysis are secondary to the carcinoma and are probably the result of the action of some toxic substance arising in the tumor and circulating in the blood. Thyroids from cancer patients showed no differences in weight or histologic structure from those found in other patients.—J. P. S.

X-ray treatment of tumors of the HYPOPHYSIS (Röntgenbehandlung der Hypophysistumoren). Kontschalowsky (M.) & Eisenstein (A.), Deutsche med. Wchnschr. (Berl.), 1922, **48**, 722-724.

The patient was a woman of 32. Three years ago **menstruation** ceased and only after treatment with **ovary** did she menstruate again. She complained of headaches and said that during the last 6-7 years her face, hands and feet had become larger. **Acromegaly,** with large **thyroid, atrophical uterus** and large sella was found. There was **polyuria** and **polydipsia.** The visual field on both sides was very small. X-ray treatment improved the visual symptoms, but had no effect on the acromegaly. The patient, however, had seizures, closely resembling epileptic fits, which were perhaps caused by the influence of x-rays on the brain. In treating tumors of the pituitary with x-rays, extreme care is necessary not to give too large quantities, as it is not yet proved that the brain is not sensitive to x-rays.—J. K.

Paroxysmal and reactional hyperfunction of the HYPOPHYSIS (Hyperhypophisie paroxystique et réactionnelle). Lévi (L.), III Réunion neurol. internat. ann., Paris, 1922; abst., Presse méd. (Par.), 1922, **30**, 605.

Physiologic causes, for instance, growth, gestation and menstruation, often bring about hypophyseal paroxysms, which are followed by morphogenetic troubles, either transitory or persistent, and to disorders of hypophyseal function. Governed by the con-

gestion or hyperplasia of the hypophysis, hypophyseal treatment may be tried.—R. G. H.

HYPOPHYSEAL dwarfism (Nanisme hypophysaire). Léri (A.), III Réunion neurol. internat. ann., Paris, 1922; abst., Presse méd. (Par.), 1922, **30**, 615.

Léri reported a case of hypophyseal nanism. The patient was 138 cm. tall, well proportioned, with normal genital organs and had had 4 children. The nanism was believed to be of hypophyseal origin because of blindness, contraction of the visual field, and modifications of the sella turcica.—R. G. H.

Dystrophia adiposogenitalis. Licsko, Klin. Wchnschr. (Berl.), 1922, **1**, 1233.

A boy of 13 years, weighing 70 kg. had bilateral atrophy of the optic nerves. No other details are given.—J. K.

(HYPOPHYSIS) Dissociated effects of lumbar puncture and of injections of retropituitrine in the polyuria of Bright's disease (Effets dissociés de la ponction lombaire et de l'injection de rétropituitrine dans la polyurie brightique). Lhermitte, III Réunion neurol. internat. ann., Paris, 1922; abst., Presse méd. (Par.), 1922, **30**, 605.

Experiments show that what is called hypophyseal polyuria is in reality caused by the lesions of the tuber cinereum. The last argument which can be invoked in the hypophyseal theory of diabetes insipidus consists of the antipolyuric effect of the injection of hypophyseal extract in such cases. But this argument is without value, because the action of retropituitrin is not entirely elective, but is equally effective upon the other secretions, as has been recently shown by the fact that antipolyuric action did not appear to be a symptom of diabetes insipidus. In patients afflicted with Bright's disease with hypertension, with Ambard's formula increased, the injection of 2 cc. of retropituitrin caused the standard of the polyuria to be raised from 5 to 2.8 litres. Moreover, contrary to what is observed in diabetes insipidus, lumbar puncture does not determine any modification of diuresis. This shows that the polyuria of Bright's disease is entirely different from that of diabetes insipidus.—R. G. H.

DIABETIC glycosuria in an old man. Subthalmic focus and unilateral alterations of the tuber cinereum. Malformation of the HYPOPHYSIS (Diabète glycosurique chez un vieillard. Foyer sous-thalamique et altérations unilaterales du tuber cinereum. Malformation de l'hypophyse). Lhermitte & Rœder, III Réunion neurol. internat. ann., Paris, 1922; abst., Presse méd. (Par.), 1922, **30**, 615.

In a patient, aged 80 years, with polyuria and glycosuria histological study revealed a focus of the right suboptic region destroying the striated projection fibres and causing a deep lesion of the tuber cinereum. The hypophysis presented a unique malformation. The hypertrophic nervous lobe did not penetrate the sella turcica, but appeared to be joined to the intervening wall, giving the appearance of an infundibular tumor.—R. G. H.

The structure and differentiation of the specific cellular elements of the pars intermedia of the HYPOPHYSIS of the domestic pig. Maurer (S.) & Lewis (D.), J. Exper. M. (Balt.), 1922, **36**, 141-156.

By use of the recent finer cytoplasmic stains the authors have demonstrated a specific type of granulation in cells of the pars intermedia. These are taken to be the true secretion antecedent for this part of the gland. The granules are smaller and stain blue and acid violet, but less intensely than any of the cells of the anterior lobe. They are very labile, disappear rapidly as a result of post-mortem change and dissolve readily in many fixing agents. The specific granules first appear in the hypophysis of embryos measuring 17.5 cm. in length, at which time Lewis has demonstrated that the fetal hypophysis first forms a pressor substance. At this stage no colloid is present in the gland. Maurer and Lewis are inclined to controvert the Herring-Cushing theory by which the secretion of the pars intermedia is held to pass into the neural lobe and on through it to the third ventricle, and thus to circulate in the cerebrospinal fluid. They hold rather that the secretion leaves the gland by the vascular route.—W. J. A.

The effect of the extract of the posterior lobe of the PITUITARY on basal metabolism in normal individuals and in those with endocrine disturbances. McKinlay (C. A.), Arch. Int. Med. (Chicago), 1921, **28**, 703-710.

In 11 out of 12 normal persons, the subcutaneous use of pituitary extract increased the basal metabolic rate quite definitely. In 4 cases of **hypothyroidism**, the interesting phenomenon occurred of a reduction in the already low basal metabolic rate following subcutaneous injection of pituitary extract. In 3 cases of disturbed function of the hypophysis, without any clinical evidence of thyroid disturbance, subcutaneous injection of pituitary extract was followed by prompt and definite rise in basal metabolism. In another group, 4 normal persons were given thyroxin and one week later, subcutaneous injection of pituitary extract. All responded by increased basal metabolic rate over and above the rate increase from the thyroxin alone. Whereas in two cases of **myxedema** whose rates had been advanced by thyroxin, subsequent injection a week later of pituitary extract had no effect. McKinley concludes that normal per-

sons and those with subnormal basal metabolism not due to thyroid deficiency, respond with accelerated heat production upon injection of pituitary extract, but that cases of hypothyroidism do not respond positively to such injection. There would seem to be a synergic action between thyroxin and pituitrin.—H. L.

DYSPITUITARISM: Report of a case of posterior lobe insufficiency controlled by organotherapy. Morris (R. S.) & Weiss (H. B), J. Am. M. Ass. (Chicago), 1922, **78**, 1522-1523.

Obesity, drowsiness, headache, frequent nocturnal urination, loss of sexual power and impairment of memory have been relieved and controlled for six years by posterior lobe extract. The detailed case report is given.—W. M. A.

PITUITARY disorders (Hypofyselidelser). Motzfeldt (K.), Norsk. Mag. f. Lægevidensk. (Kristiania), 1920, **12**, 1194-1216. (Summary in English.)

The author reports five cases. A man of 54 had for many years shown the characteristic appearance of **acromegaly**, but had felt perfectly healthy. After a severe attack of typhoid fever he developed symptoms of **diabetes** mellitus—thirst, polyuria, considerable loss of weight, muscular weakness and glycosuria, but no ketonuria. Examination revealed an enlarged sella turcica, normal fields of vision and transitory hypermetropia. He improved remarkably during dietetic treatment, and was discharged after two months. His blood sugar had gradually decreased from 0.18 to 0.11 per cent. One month later he was taken into the hospital again to have his carbohydrate tolerance tested. He could then take 500 gm. of bread and even 100 gm. of glucose without glycosuria. It seems justifiable, therefore, to consider that the man was actually cured. In a woman of 25 the usual symptoms of acromegaly had developed gradually during 7 years. The sella turcica was enlarged and the fields of vision normal. The carbohydrate tolerance was lowered. In a woman of 32 the disease was of 8 years duration; from the start there had been marked pilosity. The chief symptoms were severe headache, hemianopsia and glycosuria, but no other symptoms of diabetes. The fact is emphasized that the disturbance in carbohydrate metabolism occurs only in pituitary tumors giving rise to acromegaly. The fourth case was a man of 38 whose skin was soft, with scanty growth of hair. Adiposity had started 10 years before and sexual activity had been abolished for many years. His complaints were chiefly of a neurasthenic nature. The sella turcica and fields of vision were normal. He could take 300 gm. of cane sugar without glycosuria. **Thyroid** and especially pituitary extracts brought about marked improvement. During a relapse one month after his discharge from the hospital, considerable polyuria occurred, which disappeared spontaneously, however, after a few days duration. For the oral administration of pituitary preparations the importance

of big doses is emphasized. Adiposity in a man of 64 began 15 years ago. He has always been well and was not admitted to the hospital for his **endocrine** disturbance. The growth of hair had always been very scanty. The thyroid could not be felt distinctly. The sella turcica and fields of vision were normal. The **testes** were small and atrophic; there was no disturbance in sexual function. His carbohydrate tolerance was between 100 and 200 gm. of glucose. There was marked reaction to **adrenalin,** but no reaction to pilocarpin. It is uncertain whether this syndrome should be referred to a primary pituitary disorder or pluriglandular insufficiency.

—R. G. H.

(HYPOPHYSIS) Des troubles de sécrétion de la glande pituitaire. Pilatte (R.), Progrès. méd. (Par.), 1921, **36,** 464-465.

An historical epitome of the principal data regarding hypophyseal disorders.—R. G. H.

The action of HYPOPHYSIN, ergamine and ADRENALINE upon the secretion of the mammary gland. Rothlin (E.), Plimmer (R. H. A.) & Husband (A. D.), Biochem. J. (Lond.), 1922, **16,** 3-10.

A series of goats were used in these studies. It was found that hypophysin produces a flow of milk only in the early stages of lactation. Its action is rapid and powerful, but of short duration, and the flow then becomes less in quantity than normal. The total volume of milk per day is not altered. Since hypophysin does not act at later stages of lactation, it is probable that its action is indirect through the organs of reproduction. The chemical composition of the hypophysin milk is not different from normal. The secretory activity of the mammary gland is not affected by the subcutaneous administration of either ergamine or adrenaline. The gland probably does not contain sympathetic or parasympathetic nerve fibers for the secretory mechanism. If they be present the inaction of ergamine and adrenaline is exceptional.—F. S. H.

Studies on the effective principles in the extract of the PITUITARY body. Saito (Y.), Sei-i-Kwai M. J. (Tokyo), 1921, **40,** 4-5.

In view of discordant reports in the literature of hypophyseal pharmacology, Saito has added another experimental study. Posterior lobes of horses and cows were extracted with saline solution (1:5). From such extract the following results were obtained. It causes no dilatation of the pupil of the frog eye. There is no color reaction to iron chloride solution, but a marked reaction to Pauly's histidin. There is a vigorous contraction of a virgin guinea pig **uterus,** suspended in Ringer's solution, when a few drops of the extract are added. After the intravenous injection of the extract the rise of blood pressure is not so rapid, its maximum is much lower and the decrement is more irregular than in the case of **adrenalin**

injection. Boiling the extract in slightly alkaline solution completely destroys the pressor effect, while the depressor effect as well as the contracting action on the uterus remains undiminished. With methyl alcohol and sulphuric acid the isolated substance shows intense Pauly reaction and retains its depressing and contracting effects. After repeated extraction with chloroform of the pituitary extract, which was treated previously with trichloracetic acid, there is rise of blood pressure only on the first intravenous injection, the effect diminishing after succeeding injections at short intervals and producing even decrease. This pressor principle gives rise to the contraction of the uterine muscle, while adrenalin causes a marked relaxation of the uterus. Though a mixture of histamin and adrenalin in equal amount has about the same effect on the uterus as does pituitary extract and neutralizes its bad effects, it would be reasonable to use the pituitary extract for obstetric practice because it contains no substance inhibitory to uterine contraction.—R. G. H.

Clinical history and pathological anatomy of a HYPOPHYSEAL tumor of 14 years standing, treated by radiotherapy (Histoire clinique et anatomo-pathologique d'une tumeur hypophysaire datant de 14 ans, traitée par la radiothérapie). Sainton & Schulmann, III Réunion neurol. internat. ann., Paris, 1922; abst., Presse méd. (Par.), 1922, **30**, 615.

The histological findings are reported of a hypophyseal tumor, remarkable because of the duration of its development, and the predominance of signs of compression, contrasted with the slight endocrine reactions. There was dystrophia adiposogenitalis. Radiotherapy, which was used in 1910 led to the clinical cure of the patient, but he died of pneumonia. The tumor weighed 60 gm. It was an atypical epithelioma of the basophile cells of the anterior lobe. Although occurring at a relatively young age, this hypophyseal lesion had only a slight effect in the other endocrine glands (persistence of the **thymus**, modifications of the **thyroid**, with, finally, sclerosis and hyperplasia and **testicular** hypoplasia).—R. G. H.

ACROMÉGALIE. Secousse & Pesme, Soc. de méd. et de chir. de Bordeaux, 1922; abst., J de méd. de Bordeaux, 1922, **94**, 399.

A case of typical acromegaly is reported. Radiographs shows a thickening of the cranial structure, of the frontal sinus, of the sphenoid and of the sella. Treatment with extract of **hypophysis** has given no result; however, this is not surprising since hypophyseal hypersecretion must be present. Concomitant glycosuria diminished with continued treatment of **diabetes**, but increased in the same manner as the persistent headache with the irradiation of the hypophysis. Retinal symptoms, hemorrhages and white spots were noteworthy. Relation has not yet been established between the latter symptoms and glycosuria, but has with albuminuria and cylindruria.—R. G. H.

(HYPOPHYSIS) The influence of pituitrin on the motor function of the bladder (L'influenza della pituitrina sulla funzione motoria della vescica). Serdinkoff (M. G.), Riforma med. (Napoli), 1922, **38**, 413-417.

Following an exhaustive discussion on the action of the pituitrin on smooth muscles the author reports a case in which, besides subinvolution of the uterus (after miscarriage), peri- and parametritis, there was also inflammation of the bladder and impossibility to void urine. The condition lasted over 35 days in spite of several different treatments, electricity not excepted, and finally a positive result was obtained through injection of 0.5 cc. of pituitrin, repeated twice. The author claims a positive action of pituitrin in paresis and other functional disturbances of the bladder and suggests that fresh preparations be used to insure the desired results. Catarrhal and inflammatory conditions of the bladder should previously be treated. Pituitrin is especially efficacious in cases of acute retention due to functional disturbances of the motor apparatus.—G. V.

(HYPOPHYSIS) Specimens from the case of obesity (?), dispituitarism (?), hypernephroma, shown at last meeting. Smith (E. B.) & Donaldson (R.), Proc. Roy. Soc. Med., (Lond.), 1922, **15**, 30.

Report of post-mortem findings of a patient who was regarded by Dr. Smith as a case of dispituitarism associated with **diabetes** and as a case of hypernephroma by two of his colleagues. The patient had been admitted to the hospital to see if he would improve on a starvation diet, but instead, no reduction in sugar occurred, and there was an increase in acetone and diacetic acid. He was threatened with diabetic coma and became drowsy, so that he was put back on full diet. For 3 or 4 days he was improved; then convulsions and death occurred. The following were the post-mortem findings. There was an incipient moustache, and the hair had a feminine distribution. On the trunk, at the level of the umbilicus, the fat had a depth of 2¼ in. There were multiple small hemorrhages under the skin; the pituitary gland was normal; the **pineal** gland was small. No **thymus** could be found, but an enormous pad of fat covered both lungs. The aorta was hypoplastic. The **suprarenals** were slightly larger than normal, soft and flabby. The **pancreas** presented areas of necrosis, with areas of fat necrosis about this organ. The **testicles** were infantile and showed fibrosis with very few interstitial cells and no evidence of spermatazoa formation. A noteworthy feature was the discovery in the transverse mesocolon near the hepatic flexure of a small nodule which was regarded by the observer as an accessory suprarenal. A similar but smaller mass was found near the head of the pancreas.—I. B.

A case of HYPOPHYSEAL tumor treated by radiotherapy (Un cas de tumeur hypophysaire traitée par la radiothérapie). Souques,

Mouquin & Walther, III Réunion neurol. internat. ann., Paris, 1922; abst., Presse méd. (Par.), 1922, **30**, 615.

The authors describe a woman of 25 years who has had migraine since she was 11 years old and who has had a hypophyseal tumor for 2 years, revealed by visual hallucinations. There was temporal contraction of one visual field and blindness of the other, with optic neuritis followed by stasis and finally arrest of the menses. The sella turcica was enlarged. Radiotherapy stopped the violent headaches and the amenorrhea, but some degree of adiposity appeared.
—R. G. H.

(HYPOPHYSIS) The Mongolian idiot. A preliminary note on the sella turcica findings. Timme (W.), Arch. Neurol & Psychiat. (Chicago), 1921, **5**, 568-571.

In 23 out of 24 nonselected cases of Mongolian idiocy the radiograph of the skull showed a peculiar change from the normal in the anterior portion of the fossa pituitaria. This change consisted in an excavation of varying degrees under the anterior clinoid processes and presumably under the olivary process and optic groove, and the excavation communicated directly with the anterior portion of the fossa itself. In view of the abnormal bodily and sexual development of Mongolian idiots and of the relation of the hypophysis to development it is suggested that the author's findings point toward an etiological connection. He suggests that careful studies of the hypophysis should be made at all autopsies of Mongolians.—R. G. H.

(HYPOPHYSIS) Local asphyxia (Asphyxie locale). Van Temsch, Scalpel (Brux.), 1922, **75**, 641.

A woman of 23 showed local asphyxia of both hands with livid cyanotic color of the fingers and the nails. Pribram has described the effect of hypophysis treatment in Raynaud's disease and the author tried it in this case also with good success.—J. K.

Experimental production of GIGANTISM by feeding anterior lobe of the HYPOPHYSIS. Uhlenhuth (E.), J. Gen. Physiol., 1921, **3**, 347-365.

Metamorphosed salamanders were fed on a pure diet of anterior lobe of the hypophysis of cattle; controls were fed on earth-worms. The growth of the animals fed on hypophysis was greatly increased over that of normal animals. This growth did not cease after they had reached the normal size of the species, giants being produced. The largest animal of the species Ambystoma opacum fed on hypophysis was 19 mm. larger and of the species Ambystoma tigrinum about 28 mm. larger than the largest normal animals of these species known to the author.—H. A. McC.

Les troubles visuels dans les syndromes HYPOPHYSAIRES. Velter, III Réunion neurol. internat. ann., Paris, 1922; abst. Presse méd. (Par.), 1922, **30**, 607.

In hypophyseal disorders the ocular symptoms are of great semiologic value because of their frequency, their early development, their therapeutic importance and as true objective criteria of treatment. Statistics of Uthoff show that out of 207 cases of **acromegaly** there were more than 100 cases of bitemporal hemianopsia, but only 11 cases of papillary stasis. The statistics of Cushing and of Lapersonne are concordant. There are several semipathognomonic symptoms of lesions of the basal region. By far the most important are the changes in the visual field. Bitemporal hemianopsia shows a lesion of the chiasm. Generally the lesions are unequally distributed. The deficit of the temporal fields is not symmetrical. The central vision is usually spared, with the exception of the loss of the macular field. The pupillary troubles are variable. The most common is pupillary inequality with conservation of the light reflex. The hemianoptic reaction of Wernicke is exceptional. A discordance exists between functional troubles and lesions ascertained by the ophthalmoscope, which often does not show anything but decoloration of the papilla on the temporal side. In 15% of the cases papillary stasis exists due to hypertension. Visual acuity is connected with statsis or atrophy. Oculomotor troubles as well as exophthalmos are connected with lesions of the base. It is the chiasmic syndrome which is most characteristic, demands diagnosis and renders especially important radiography of the sella turcica. Radiotherapeutic treatment has often given excellent results upon visual disorders.—R. G. H.

(HYPOPHYSIS) Glycosuria in pregnancy. Wallis (R. L. M.), Proc. Roy. Soc. Med. (Lond.), 1922, **15**, 31-32.

Special attention was directed to the mild type of the condition, rather than to severe glycosuria. Plotting out the curves, they were found identical with those in hyperpituitarism, suggesting that the **pituitary** plays some rôle in pregnancy.—Physiol. Abst., **7**, 252.

Classification and etiology of INFANTILISM (Ueber Abgrenzung und Entstehungsursachen des Infantilismus). Borchardt, Deutsches Arch. f. klin. Med. (Leipz.), 1922, **138**, 129-143; Deutsche med. Wchnschr. (Berl.,) 1922, **48**, 406.

Infantilism is a real retarded development, a kind of "subevolutionism," which in growing persons produces a state of mind and body belonging generally to much younger persons. Adults with infantilism have a state of mind and body much less developed than normally. The author proposes a classification as follows: hereditary infantilism; infantilism due to harmful effects on ovum or spermatozoon (alcohol, lead, x-rays); endocrine infantilism (dys-

thyreogeneous, **hypophyseal** and **pluriglandular** infantilism); and dystrophic infantilism (from early infection, such as **intra-uterine, syphilis,** tuberculosis, etc., from defective feeding, from use of alcohol in childhood, and from congenital or early developed heart disease).—J. K.

Epidemiological and clinical contributions on malarial INFANTILISM (Contributo epidemiologico e clinico sull' infantilismo malarico). Chimisso (L.), Riforma med. (Napoli), 1922, **38,** 241-243.

Report of a few cases of malarial infantilism found in Campomarino (Molise-So. Italy), a region infested by malaria. The population, originally Albanian, immigrated to Italy about 1460. It is a striking example of degeneration, caused by malaria, of a once tall and powerful race. A big splenic tumor is always found in these cases of real infantilism; and Prof. Cardarelli quotes an interesting case in which, after removal of the spleen, the infantilism has been cured.—G. V.

Action of LYMPHATIC gland extract on blood cells (L'azione delle ghiandole linfatiche sulla costituzione morfologica del sangue). Galera, Gior. di Clin. med. (Parma), 1922, **3,** 1-4.

The author, bearing in mind the connection between lymphatic glands and white blood elements, and also between these and the loss of virulence of the Koch bacillus in animals, seeks to ascertain whether a similar action is possible on the living blood of man by means of calf gland extract. The glands were reduced to a thin pulp, mixed with an equal part of physiological saline solution and shaken. After about an hour's refrigeration the mixture was passed through a filter and sterilized in an autoclave at 110° C. Injections of 5 cc. of extract were made on alternate days in patients suffering from pulmonary or peritoneal tuberculosis. The blood was examined before the injection, and also 4, 24, and 48 hours afterwards. The following approximately constant modifications were seen: leucocytes after 4 hours, increase of 3000 to 4000, less at the 24th hour, and normal at the 48th; eosinophiles and basophiles, without modification in their number; lymphocytes, increase of 10 to 15 at the 4th hour and from the 24th diminution, attaining normality at the 72d; large mononuclears only slightly increased.—P. M. N.

Carbohydrate metabolism in diseases of the LIVER (Kohlenhydrathydrat-Stoffwechsel der Leberkranken). Heténi (G.), Deutsche med. Wchnschr. (Berl.), 1921, **48,** 420.

In diseases in which the quantity of parenchyma is decreased the formation of sugar in the liver is decreased also. When the bile passages are obstructed the formation or the fixation of glycogen in the liver is diminished. Diseases of the parenchyma cause a low amount of blood sugar; when the bile passages are obstructed the

blood sugar is often increased. However, in diseases of the parenchyma, compensatory hypertrophy may neutralize its influence. As concomitant lesions of the pancreas may also have a complicating influence the authors conclude that blood sugar determinations have but little value in the diagnosis of diseases of the liver.—J. K.

Carbohydrate metabolism in diseases of the LIVER (Kohlenhydratstoffwechsel bei Leberkranken). Hétényi (G.), Deutsche med. Wchnschr. (Berl.), 1922, **48**, 770-771.

When 100 gm. of glucose are ingested on the empty stomach there is always a rise of blood sugar. This rise is much higher in diseases of the liver than in other diseases. If the rise is not over 40% the liver is probably not diseased. When it is found in healthy persons it is probable that the liver function has suffered from the war. The function of the liver cannot be determined by the alimentary glucosuria for that depends upon the function of the kidneys. —J. K.

(LIVER) Cardio-vascular effects of hepatic extracts (Les effets cardio-vasculaires des extraits hépatiques). Roger (H.), Presse méd. (Par.), 1922, **30**, 441-445.

Roger demonstrated the presence in the liver of substances which influence the blood pressure and the heart action in opposite directions. He used intravenously on dogs and rabbits extracts of liver tissue obtained by autolysis, by sulfuric acid and by alkaline (barium) hydrolysis. (The work is a continuation of the experiments with extracts of renal tissues, which were published in the Presse méd., 1918 and 1921.) The concentration, the rapidity of injection, and the method of extraction were found to influence the character of the reactions obtained. In order to abolish the effect of peptones in the extracts, Roger used precipitation with alcohol, with ether or with bichloride of mercury after treatment in vacuo; the residue was taken up saline solution. (Detailed data on the chemical procedures and many tracings on blood pressure and cardiac action are given in the original.) Roger believes that the extracts contain several substances, of which the isolation may prove to be very difficult, as they are likely to be altered or destroyed in the process. He succeeded, however, in isolating a substance which chiefly influences the action of the heart; its effects were studied with the electrocardiograph, and the findings compared with those following injections of atrophine sulfate, while the immobility of the animal was assured by very small amounts of morphine, which, alone, did not affect the heart. The extracts secured by alkaline hydrolysis gave the most interesting results; they produced sinus-bradicardia, and, notwithstanding the constriction of the blood vessels which should have caused hypertension, a marked fall of the blood pressure. Roger believes that some of these substances may play a part, perhaps normally, but especially in cardio-hepatic dis-

turbances, by their introduction into the blood stream in minute amounts following cell destruction, as they occur in extracts obtained by autolysis. He thinks that the alkaline, etherized extracts may prove to be of therapeutic value when the method of extraction has been perfected, because they act selectively on the heart and the blood vessels.—G. L.

The OVARIAN CYCLE and its influence upon uterine changes (Der Ovarialcyclus und sein Einfluss auf die Veränderungen des Uterus). Schröder (R.), Klin. Wchnschr. (Berl.), 1922 (Feb. 25), **1**, 403-405.

An excellent review, without new facts, of the chronological relationships between the ovarian and uterine changes at the various phases of the menstrual cycle.—J. K.

An accessory PANCREAS in the wall of the gall bladder of a dog. Mann (F. C.), Anat. Record (Phila.), 1922, **23**, 351-353.

A small pancreas, located immediately under the serosa of the gall bladder, is described. There was no connection with the major pancreas. Three small ducts emptied directly into the gall bladder. A few definite but very small islands were found in the accessory gland.—W. J. A.

An attenuated form of hepato-PANCREATIC cirrhosis with bronze DIABETES (Une forme attenué de cirrhose hépato-pancreatique avec diabète bronzé). Labbé (M.) & Stévenin (H.), Bull et mém. Soc. méd. des hôp. de Par., 1922, **46**, 785-788.

A report of a mild case of bronze diabetes lasting for two years and terminating by gastric cancer.—F. S. H.

Clinical and pathological TETANY (Beiträge zur klinik und Pathologie der Tetanie). Elias (H.) & Weiss (S.), Wien. Arch. f. innere Med., 1922, **4**, 59-64.

Elias and Spiegel confirmed their former convictions that in tetany there is an increase in the inorganic and the total phosphorus. When the tetany becomes latent the quantity of phosphorus does not become normal, but for some unknown cause may become even higher.—J. K.

(PARATHYROID) Postoperative TETANY. Kaposi, Klin.Wchnschr. (Berl.), 1922, **1**, 1334.

No details are given.—J. K.

The influence of PARATHYROIDECTOMY on the skeleton of animals normally nourished, and on rickets and osteomalacia produced by deficient diet. Korenchevsky (V.), J. Path. & Bacteriol. (Cambridge), 1922, **25**, 366-392.

These experiments were made on 35 rats, from 21 of which the parathyroids had been successfully removed. The remaining 14

served as controls. Parathyroidectomy produced no marked effect on the skeleton of rats kept on normal or ricket-producing diets. Vitamin A has an important relation to the metabolism of calcium in the organism and particularly in the bones and to the etiology of rickets or osteomalacia. The changes typical of rickets or osteomalacia occur most readily and most frequently in rats kept on a diet deficient in both vitamin A and calcium. Parathyroidectomy affects the teeth, as shown by Erdheim, but diets deficient in calcium, vitamin A, or in both these factors, also produce apparently analogous changes. Rickets was produced in rats provided the age was not greater than 3 to 5 weeks at the beginning of the feeding. When the special feeding started at the age of about 2 months, a picture characteristic of late rickets or osteomalacia juvenilis resulted, namely, the changes in proliferating cartilage was not well marked. Korenchevsky believes, therefore, that there is no essential distinction between rickets and osteomalacia, the only modifying influence being age.—J. P. S.

The importance of the PARATHYROIDS and the treatment of postoperative tetany (Die Bedeutung der Epithelkörperchen und die Behandlung der postoperativen Tetanie). Landois (F.), Ztschr. f. ärztl. Fortbild. (Jena), 1922, **19**, 321-325.

A general review. For treatment of postoperative tetany parathyroid tablets and calcium lactate up to 30 gr. daily are given—when necessary intravenously. When possible a graft is made. If all the parathyroids are ablated, the author thinks any treatment is absolutely useless.—J. K.

Transplantation of PARATHYROID in general and as a treatment of especially Parkinson's disease (Über die Verpflanzung der Nebenschilddrüse im allgemeinen und alstbittelgegen Paralysisagitans im besonderen). Madlener (M.), Zentralbl. f. Chir. (Leipz.), 1922, **49**, 703-705.

In 16 operations for goiter the author removed small pieces of tissue, which he believed to be parathyroids. A real parathyroid was found only 5 times. Borchers (Endocrin., **5**, 375) is right when he states that no transplantation should be made without histological examination. Even though the graft does not continue to live, such a transplantation may be extremely useful in cases of temporary parathyroid insufficiency. Most grafts are for postoperative **tetany**; only once has the operation been carried out for Parkinson's disease (Küll). The author performed a transplantation in a man of 52 who suffered for 7 years from paralysis agitans. Three days after the operation the rigidity of the muscle was diminished, though the tremors continued. After 3 weeks the patient was markedly better, but 6 weeks later all symptoms had returned. An unknown quality perhaps exists so that it is of importance to continue trying the graft in other new cases.—J. K.

PARATHYROID coma (Das Parathyreoprive Koma). Melchior (E.), Zentralbl. f. Chir. (Leipz.), 1922, **49**, 667-669.

Some time ago Melchior described a form of coma after ablation of the **thyroid.** He gave the following proofs to the effect that it was due to a loss of parathyroid function. Severe **tetany** may end in coma. Many years ago Schiff discovered that complete ablation of the thyroid sometimes produced coma and we now know that this would not be caused by a loss of the thyroid itself. Stankovic has described many soldiers (without operation) dying in coma with positive symptoms of Trousseau and Chvostek. In medical literature many unexplainable cases of death in coma after large resections of **goiter** are described. Mann has described a patient who showed a severe coma after removal of a goiter and ligation of the four arteries. This patient had formerly had epilepsy and a relation between epilepsy and tetany is claimed. The coma after ablation of the thyroid is of parathyroid origin.—J. K.

Neurotic TETANY due to respiration and the treatment of tetany with ammonium phosphate (Über neurotische Atmungstetanie und über die Behandlung der Tetanie mit Ammonphosphat). Porges (O.) & Adlersberg (D.), Klin. Wchnschr. (Berl.), 1922, **1**, 1200-1201.

Vernon was the first author to describe the outbreak of tetany after exaggerated respiration. He examined some patients with very deep breathing, showing tetanic symptoms. Grant and Goldman state that in deep respiration the blood loses CO_2, and shows a more alkaline reaction. In this way the calcium salts become less soluble, thus causing tetany. The best treatment, therefore, is to increase the acidity of the blood. This may be attained by carbohydrate free food, inspiration of air mixed with CO_2, muscular work, and administration of ammonium salts of inorganic acids. All of these methods are successful. As a salt of ammonium the phosphate is recommended, since the chloride is not palatable.—J. K.

TETANIE. Porges (O.) & Adlersberg (D.), Wien. klin. Wchnschr., 1922, **35**, 235-236.

Vernon discovered some 10 years ago that persons showed all symptoms of tetany after energetic and slow respiration. Two patients were examined. One, a nervous woman with perhaps a tumor of the lungs and of a kidney, began to breathe very hard during a cystoscopy. She developed a typical attack of tetany. The other patient showed an increased respiration during a lumbar puncture and had a tetanic fit also. When the patients' respiration was normal they did not show any symptoms of latent tetany. The authors state that during exaggerated respiration the blood loses CO_2 and becomes more alkaline and the calcium of the blood may be partly changed to a less soluble form. In this way respiratory

tetany may also be explained as caused by a decreased calcium content.—J. K.

(PARATHYROIDS) Tincture of hyoscyamus and hyoscin in Parkinson's disease: effect on tremor and sleep (La teinture de jusquiame et l'hyoscine dans la maladie de Parkinson: influence sur le tremblement et le sommeil). Rebattu, Mollon et Sédaillen, Presse méd. (Par.), 1922, **30**, 241.

Rebattu, Mollon and Sédaillan reported satisfactory results from the use of tincture of hyoscyamus combined with hyoscin in several cases of Parkinsonia, in athetosis and in chorea. (Meeting of the Soc. méd. des hôp. de Lyon.) They made the following observations: Injections of hyoscin alone are dangerous and difficult; symptoms of intoxication occurred with 0.5 mg.; the effects on tremor and sleep are transient. Administration of hyoscin by mouth (maximum dose, 1 mg.) is less dangerous; sleep improves, but the tremor is affected little. The combination of hyocyamus with hyoscin caused both tremor and pains to disappear entirely for three days in one patient, who also slept much better. Tincture of hyocyamus alone diminishes the tremor and the pains to a certain extent, causes the patients to sleep better and improves their general condition. Contrary to Erb's observations hyoscin does not seem to be contra-indicated by cardiac lesions; it was used without producing any untoward effects in a patient with mitral insufficiency, and for another patient with a "persistently slow pulse." The authors conclude that, since the combination of tincture of hyocyamus with hyoscin controls the tremor, abolishes the pain, in duces sleep and promotes well-being without untoward effects, this method of treatment offers advantages and should be given a further trial. (The dosage of the tincture of hyocyamus is not given.)

—G. L.

Histology and physiology of the human PINEAL GLAND (Zur Histologie und Physiologie der menschlichen Zirbeldrüse). Walker (F. K.), Ztschr. f. d. ges. Neurol. u. Psychiat. (Berl. & Leipz.), 1922, **74**, 314-330.

The paper deals specifically with the large cells with smooth knob-like process found in the perivascular tissue of the pineal gland. The author concludes that these cells are specific elements and not glia cells nor nerve cells. Hyperplasia of these cells is described in four cases of brain tumor with distinct intracranial pressure. In two cases of congenital hydrocephalus without pressure symptoms this hyperplasia was not in evidence, although in one case the gland was greatly enlarged. He explains the atrophy (one case) or entire absence (two cases) of the pineal gland in congenital hydrocephalus which he found in one year old children with marked pressure symptoms as being due to secondary atrophy produced by the excessive pressure of the cerebrospinal fluid, there

having, in all probability, first been the usual hyperplasia. These observations he thinks strengthen his earlier idea that the pineal gland may act as a reflex center governing the secretion of cerebrospinal fluid and hence intracranial pressure. He hopes to be able to report soon on an abundance of clinical material along this line. Some literature is given.—A. T. R.

Indications for the removal of the SPLEEN in infants and children. Bartlett (F. H.), Am. J. Dis. Child. (Chicago), 1922, **23**, 283-309.

Bartlett collected the reports of all previous splenectomies under 14 years of age, amounting to 51 cases. He adds 3 to the literature. In studying and analyzing the cases reported and his own, he comes to the following conclusions. The conditions for which relief or cure by splenectomy may be indicated are present in the first 5 years of life more frequently than is generally accepted. It is desirable to remove the spleen in the early stages of the pathological process for which splenectomy is indicated. Hemolytic jaundice presents the most favorable condition for splenectomy. Banti's disease and Gaucher's disease represent pathological processes for which splenectomy may give relief of symptoms and may serve to prolong life. Von Jaksch's disease is probably not an independent condition. Indications for the removal of the spleen depend upon certain criteria, not on the making of a definite diagnosis; these criteria are splenomegaly, secondary anemia, and the failure of repeated blood transfusions to determine any improvement in the anemia and general condition.—M. B. G.

A clinical and radiographic study of the THYMUS in infants. Blackfan (K. D.) & Little (K.), Am. J. Dis. Child. (Chicago), 1921, **22**, 459-471.

Sixty patients without symptoms referable to the thymus were examined with particular reference to percussion dulness and to the roentgenray shadow of the thymus. They ranged in age from 5 hours to one year. They regarded the thymus as "negative" if dulness extended not over seven-eighths of an inch to the left, if there was no dulness, or if it was not over half an inch to the right of this point. Dulness in the second interspace both to the right and the left of the midsternal line and continuous with the cardiac dulness below was regarded as a "positive" thymus. Disappearance of dulness with the head in extreme dorsal flexion was confirming evidence. In the "positive" thymus, the x-ray shadow in the anterior mediastinum was either continuous with the heart shadow, obliterating the normal cardiac angles, or it was superimposed on the heart shadow as a broad cap. Thirty-one of the 60 patients failed to show a shadow in the anterior mediastinum, indicative of the thymus. Twenty-nine showed a shadow which was indicative of the thymus. A comparison of the roentgen ray findings and the physical findings show that 27 patients were negative both with the x-ray and on per-

cussion; 20 patients were positive both with roentgen ray and on percussion; 4 were negative with the x-ray and positive with percussion; 9 were positive with the x-ray and negative on percussion. In 6 infants who showed clinical symptoms of enlarged thymus on percussion there was found an increased dulness to the right and left of the midsternal line in the second interspace, which was continuous with the cardiac dulness. In each patient the roentgenogram revealed a shadow in the anterior mediastinum indicative of enlarged thymus. In an analysis of over 200 x-ray pictures it proved impossible to find any points of differentiation between the roentgen ray shadow found in patients with the clinical symptoms of enlarged thymus and the thymus shadow in "normal" infants. They believe that a shadow in the anterior mediastinum which does not show any diminution in size after intensive roentgen ray therapy is not the shadow of the thymus. In case of the doubt roentgen ray treatment should be administered. In one patient it was found that percussion dulness as obtained after death corresponded closely to that during life, that this area of dulness was identical with the shadow cast by the roentgen ray and that the difference of the shadow cast before death and after death was very slight. They felt that the shadows cast in this series should be recognized as due to the thymus since it disappeared after x-ray treatment, it could not be distinguished from the shadow which at necropsy was proven to be cast by the thymus and that it was identical with that found in patients with clinical evidence of enlarged thymus.—M. B. G.

(THYMUS) Respiratory obstruction resulting in death. Bruce (J. W.) & Graves (S.), Am. J. Dis. Child. (Chicago), 1922, **23**, 438-441.

A case is reported of a boy 4 months of age whose illness dated from the day after his birth when his mother noticed that his breathing was more noisy than normal. This noisy breathing became more and more pronounced. He had been cyanotic only once for about five minutes when he seemed to strangle. Even though physical examination and roentgenograms of the chest showed no abnormality, a diagnosis of enlarged thymus was made and roentgen ray treatment at one week intervals for four weeks was instituted. For 48 hours after each treatment his condition was worse, the stridor becoming more pronounced, the breathing more difficult and cyanosis present. He was not benefited by the x-ray treatment. About one week before his death, his condition became worse, respiratory difficulty and cyanosis being almost constant. Necropsy revealed nothing unusual except malnutrition and an unusual shape and location of the thymus. It was 3 gm. in weight, situated 10 mm. above the sternoclavicular joint and roughly triangular in shape. No other reason being apparent the authors feel that the enlarged thymus was the cause of death.—M. B. G.

The action of soft x-rays upon the THYMUS. Erlichówna (Marta), Trav. du lab. de l'inst. M. Nencki, 1921, **3**, No. 1; reprint 23 pp.

Soft x-rays (½ to 2 H) produce in the thymus (rabbit) a somewhat less marked degeneration and cellular destruction than the hard rays (10 to 50 H). The general effects are moderate anemia, loss in body weight, and an increase in the albumin in the blood as determined refractometrically. These effects are considered to be due to the poisonous action of the degenerating thymus. X-ray therapy has its dangers.—Physiol. Abst., 1922, **7**, 194.

THYMUS development (Die Entwicklung der Thymus beim Rind). Hagström (M.), Anat. Anz. (Jena), 1921, **53**, 545-566.

Of morphological interest only.—A. T. R.

(THYMUS) Evidence for the existence of lymphatism in suicide cases (Zur Prüffung des Lymphatismus des Selbstmörders). Hammar (J. A.), Vrtljschr. f. gerichtl. Med. (Berl.). 1917, **53**. 217-236.

Data from accurate quantitative analyses of the thymus in 18 cases of suicide between 17 and 35 years of age were compared with similar determinations on the thymus of 17 accident cases from 16 to 35 years of age; there was found no morphological evidence for the idea that the thymic parenchyma is supranormal in amount in suicide cases. Neither the whole thymus, cortex, medulla nor proportion of cortex to medulla ("index") was larger in the cases of suicide than in the accident cases with sudden death. In 5 out of the 18 suicide cases the parenchyma was below the lowest found in any accident case. Hassall's corpuscles were irregular. In 11 suicide cases the absolute and the relative number of corpuscles were less than the average of the accident cases and in 6 cases even less than the smallest number found in the accident cases.—A. T. R.

Further elucidation of the structure of the THYMUS in so-called thymic death: microscopical analysis of the thymus in 24 cases of mostly sudden death from internal causes (Zur ferneren Beleuchtung der Thymusstruktur beim sogen. Thymustod: mikroskopische Analyse der Thymus in 24 Fällen meistens plötzlichen Todes aus inneren Gründen). Hammar (J. A.), Ztschr. f. Kinderh. (Berl.), 1917, **15**, 225-312.

An exhaustive quantitative analysis of these thymi gave no evidence of any abnormality beyond that seen in cases which have met accidental death from external causes. Medullary hyperplasia was no more frequent in cases diagnosed as "thymic death" than in accident cases of similar age. The thymus seemed in no way to have been involved as a factor which could cause death. The cause of death in these cases, he thinks, must evidently be looked for elsewhere, mostly likely in other organs of internal secretion.

—A. T. R.

Microscopical analysis of the THYMUS in 25 cases of acute infectious diseases (acute anterior poliomyelitis, scarlatina, measles, whooping-cough, typhoid fever and in one case each of starvation and snake bite) [Verhalten der Thymus bei akuten Infektionen: mikroskopische Analyse der Thymus in 25 Fällen von akuten Infektionskrankheiten (Poliomyelitis anterior acuta, scarlatina, morbilli, pertussis, typhus abdominalis). Als Anhang: Die Thymus bei einen Todesfall durch Hunger und einen durch Schlangenbiss]. Hammar (J. A.). Ztschr. f. ang. Anat. [etc.] (Berl.), 1918, **4**, 1-107.

A very detailed quantitative analysis with the following results: Poliomyelitis (11 cases) presented a thymus variable in size but generally within normal limits, but invariably with an absolute and relative increase in the number of small Hassall's corpuscles. A few cases showed more or less accidental involution. The 9 cases of scarlatina were characterized by marked accidental involution with a large increase in the number of small Hassall's corpuscles. The 3 cases of measles and single case of pertussis showed also marked involution and numerous small corpuscles. The parenchyma of the thymus in the typhoid fever case was distinctly subnormal in amount, but large Hassall's corpuscles were overabundant. The starvation case (due to congenital pyloric stenosis) agreed well with experimental inanition effects on the thymus, there being reduced parenchyma and high relative but low absolute number of Hassall's corpuscles. In the case of the snake bite the picture was essentially like that in most of the above acute infections (marked involution and increase in small corpuscles), except that there was more calcification. Graphs, literature, etc., are given.—A. T. R.

Microscopic analysis of the THYMUS in a number of cases of congenital lues (Beiträge zur Konstitutionsanatomie VII. Mikroskopische Analyse der Thymus in einigen Fällen von Lues congenita). Hammar (J. A.), Beitr. z. path. Anat. u. z. allg. Path. (Jena), 1919, **66**, 37-91; 195-258.

This paper deals with the detailed quantitative histological examination of the thymus in 11 cases of congenital lues and one questionable case. As a direct result of the syphilitic infection the author found one case with a Dubois abscess and in all cases a high degree of lymphocytic infiltration of Hassall's corpuscles; but these changes are not considered entirely differential for congenital lues. Hypoplasia and accidental involution are considered indirect results of syphilis. An increase in connective tissue, thickening of the adventitia of blood vessels and the presence of "epithelioid" cells are not considered organ changes that are specific for congenital lues. Extensive literature is reported.—A. T. R.

Microscopical analysis of the THYMUS in 25 cases of Graves' disease (Beiträge zur Konstitutionsanatomie. I. Mikroskopische

Analyse der Thymus in 25 Fällen Basedow'scher Krankheit). Hammar (J. A.), Beitr. z. klin. Chir. (Tübing.), 1917, **104**, 469-614.

In 18 cases of Graves' disease the thymi were found to have a supranormal amount of parenchyma; in 7 cases the parenchyma was normal or subnormal. In all cases where the total weight of the gland was above the normal, the parenchyma was supranormal, and it was so in 4 cases where the total weight fell within the limits of normal variation. When hyperplasia of the thymus took place the cortex was always involved. The medulla was supranormal in some cases, but not in all. Where both cortex and medulla are supranormal the cortex exhibits the greater increase. There is always an increase in the number of Hassall's corpuscles, both in the total number and in the number per mg. of parenchyma. The smaller corpuscles are especially plentiful and calcified corpuscles are almost entirely lacking. These conditions are found also in the thymi which show a normal or subnormal amount of parenchyma. The small size of these last is probably due to an accidental involution. Since the thymi in Graves' disease do not resemble those of the infantile type nor those found in cases of thymic death or "status lymphaticus" the author concludes it is more accurate to call the condition one of hyperplasia than of subinvolution, persistence or revivescence. The enlargement of the parenchyma seen in these cases was not unlike that found in other conditions, but the number and kind of Hassall's corpuscles are peculiar to Graves' disease. The organs were studied by the projection method used by the author in earlier work on the thymus. A greater accuracy in measuring the total amount of parenchyma and the relative amounts of cortex and medulla is secured by this method. The use of other methods, such as measuring by eye, has led to the frequent reports of medullary hyperplasia in Graves' disease. Another source of error has been eliminated in this work by comparing each gland with a number of thymi of the same age, instead of using the infantile thymus as the norm.—M. M. H.

A contribution to the topographic anatomy of the THYMUS gland with particular reference to its changes at birth and in the period of the new-born. Noback (G. J.), Am. J. Dis. Child. (Chicago), 1921, **22**, 120-145.

The thymus was studied in the cadavers of 65 fetuses and full term children by means of dissection, graphic reconstructions and freehand sections. No material was used in which pathological conditions were macroscopically observable. The lobation of the thymus is determined early in fetal life and the establishment of respiration obviously has no effect on it. The thymus in the late fetus and in the new-born is predominantly of the cervicothoracic type. The thymus in the late fetus and stillborn child has a typical

form and quite constant relations. Its lateral surfaces are convex and bulge against the medial surfaces of the lungs. The lungs very rarely extend at all on its anterior surface, and the thymus very rarely extends at all on the anterior surface of the right ventricle of the heart. The thymus in liveborn infants has typical form and relations which are similar to those found in young children. It is elongated and molded so that its anterior, lateral and posterior surfaces bear the impress of all the organs with which it is in contact. Its lateral surfaces usually show marked convexities which are occupied by its lungs which pass over the anterior surface of this organ. Unlike the fetal thymus, it usually extends more inferiorly passing over the right ventricle. The change from the broad or fetal type of thymus to the elongated and molded type found in the liveborn bears a direct relation to the establishment of respiration and is dependent on the expansion of the lungs. The organ is compressed from side to side by the medial surfaces of the expanding lungs. It is compressed anteroposteriorly by the anterior borders of the lungs which become more thickened early in the establishment of respiration as they gradually overlap the thymus.—M. B. G.

X-ray treatment of the THYMUS in psoriasis (Zur Thymusröntgenbestrahlung bei Psoriasis). Schneider (P.), Wien. klin. Wchnschr., 1922, **35**, 565-566.

Brock has advocated the treatment of psoriasis by x-ray treatment of the thymus. Schneider tried this treatment in 12 cases and a good effect was seen only twice. It has not yet been proved that there is a relation between the thymus and psoriasis.—J. K.

Epitheliomata of THYMIC origin. Symmers (D.) & Vance (B. M.), Arch. Int. Med. (Chicago), 1921, **28**, 239-251.

Only three examples of primary thymic epithelioma are to be found in the literature. A fourth is recorded in this paper. The lymphocytic tumors far outnumber the epithelial and occur usually at a younger age. Intrathoracic pressure signs are inconstant; in some cases negligible, in others very severe and quite sudden in onset. Lymphosarcoma of the thymus, as elsewhere, invades adjacent tissue, but metastasis is apt to be a late event. The lymphoid growths should be benefited by the roentgen ray.—H. L.

THYMUS apoplexy. An unusual manifestation of hemorrhagic disease of the newly born. Wahl (R. N.) & Walthall (D.), Am. J. Dis. Child. (Chicago), 1922, **24**, 27-44.

Because of the rich blood supply, the thymus is apt to become congested, especially whenever there is general circulatory stasis. Hemorrhage may be scattered, small and petechial in character or it may appear as large effusions of blood localized or diffused throughout the substance of the organ. The former are common, especially

in asphyxial conditions in acute infections and in hemorrhagic diseases. The latter, to which Friedleben gave the name of "Apoplexien" are relatively rare. Such an "apoplexy" may follow hyperemia associated with simple hyperplasia of the gland and may give the appearance of a hemorrhagic infarct. They usually occur in very young infants or the new born and are often associated with sudden death. The etiology of the condition is obscure but seems to be associated with syphilis more than with any other factor. Circulatory stasis, trauma, nonspecific infections and hemorrhagic tendency are contributing, if not the main factors in some cases. There is no way of making a clinical diagnosis. The authors analyse the 19 cases in the literature and add two of their own. Their cases occurred in children 4 days and 6 weeks old, respectively. Both showed symptoms of meningeal irritation, lateral nystagmus, generalized icterus, marked increase in the coagulation time of the blood, and hemorrhage. Labor, while not normal, was not unduly difficult or prolonged in either case. In each case, the necropsy findings showed a cerebral hemorrhage, inflammatory changes in the lungs suggestive of syphilis and a diffuse hemorrhagic infiltration of the thymus in which the extravasation of blood was both intralobular and interlobular and was associated with suppuration, necrosis and marked proliferation of the reticular epithelial cells.

—M. B. G.

The chemical composition of the THYMUS and the relation by weight between this organ and the THYROID (Recherches sur la composition chimique du thymus et sur les rapports pondéraux entre cet organe et le corps thyroïde). Zunz (E.), Arch. intern. de physiol. (Liége & Par.), 1920, **15**, 459-472.

It is exceptional to observe considerable atrophy of the thymus in the healthy adult man (soldier killed in war). The average weight of the thymus in man from 19 to 34 years is 15 to 16 gm. The maximum surpasses 30 gm. In spite of great individual variation, the percentage of material extracted by ether tends to increase with age. The weight of the whole fresh thymus which has been extracted by ether and then dried tends to be increased more when the weight of the thyroid is less. It is always less than that of the thyroid gland when the latter weighs more than 29 gm. in the fresh state. It is greater than that each time the thyroid weighs less than 19 gm. The content of the thymus gland, the dry residue, the nitrogen, the phosphorus and the ash does not appear to have any relation whatever to the age of the subject, to the weight of the fresh thymus or to the weight of the thyroid gland. The chemical composition of the thymus among healthy adults is relatively constant. The phosphorus lipoid of the thymus is relatively constant, but the quantity present is not great.—Physiol. Abst., **6**, 71.

(THYROID) Substances with specific action prepared from single organs. IV (Studien über die von einselnen Organen hervorgebrachten Substanzen mit spezifischer Wirkung. IV). Abderhalden (E.) & Schiffmann (Olga), Arch. f. d. ges. Physiol. (Berl.), 1920, **183**, 197-209.

The corresponding effects of (a) fresh normal human thyroid, (b) cattle thyroids hydrolysed by sulphuric acid, the hydrolysate evaporated to dryness, extracted with absolute alcohol, and the extract evaporated under diminished pressure, the residue being dissolved in 100 times its volume of water, (c) the aqueous preparation corresponding to (b) soluble in dilute alcohol, and (d) the corresponding aqueous solution of the residue insoluble in dilute alcohol, were tested on tadpoles of Rana temporaria and Bufo viridis. The effects of all four were similar in kind, (c) being stronger, (b) and (d) weaker than (a). The most marked effect is on the intestine. The shortening takes place more rapidly; clumps of degenerated epithelial cells are more noticeable; its metamorphosis begins earlier. The growth of the **pituitary** is lessened. No very definite results were obtained on the thyroid and **thymus.**—A. T. C.

(THYROID) Studies on substances with specific action prepared from single organs. VIII (Studien über die von einzelnen Organen hervorgebrachten Substanzen mit spezifischer Wirkung. VIII). Abderhalden (E.) & Schiffmann (Olga), Arch. f. d. ges. Physiol. (Berl.), 1922, **195**, 167-198.

When toad-tadpoles of differing ages are treated with fresh thyroid, the younger animals show the growth-inhibition and metamorphosis acceleration more slowly, become more deformed and die before the end of metamorphosis. Older animals react more rapidly and show the effect of thyroid typically. Colloid and exophthalmic goitres produce no, or but slight, action on toad-tadpoles. Thyroids hydrolysed with sulphuric acid act on them but weakly, but have a typical action on Rana temporaria tadpoles. Di-iodo-tyrosine and di-iodo-tyramine act on Bufo and on Rana in the same way as thyroid. The earlier the treatment the stronger is the action. Glycyl-di-iodo-tyrosine, and di-iodo-tyrosine methyl ester produce the same action as di-iodo-tyrosine. Iodo-acetyl-di-iodo-tyrosine, β-iodo-propionic acid, alival, and tyrosine are without action.—A. T. C.

Nocturnal (paroxysmal) dyspnea: its treatment with THYROID gland. Adams (R. D.), J. Am. M. Ass. (Chicago), 1922, **78**, 1876-1877.

The discussion is confined to those cases in which the cardiovascular system dominates the picture, as myocarditis, aortic disease and arteriosclerosis. The cause of these attacks is discussed. By treating with thyroid gland 15 patients averaging 52 years of age, 12 were distinctly relieved, 2 were unaffected and 1 was un-

favorably influenced. The relief following the administration of iodides may be due to thyroid stimulation.—W. M. A.

(THYROID) Nutritional needs in myxedema (Der Nahrungsbedarf beim Myxödem). Ambrozic (M.), Ztschr. f. Kinderh. (Berl.), 1921, **29**, 117-126.

In studies of nutrition of children with myxedema, thyroidin therapy was used and the conditions found are expressed in terms of v. Pirquet's formula. The demand during periods when thyroidin was withheld amounted to between 30 and 40 "centinemsiqua"; during periods of thyroidin therapy it was always higher, varying between 40 and 67 cnsq., with limits of 37 to 98 cnsq. The thyroidin therapy in average doses increased the demand about 15 to 20 cnsq.; larger amounts gave a correspondingly great difference.

—Chem. Abst., **16**, 739.

THYROID and parathyroids in animals kept in the light or in the dark (Schilddrüse und Epithelkörperchen bei Licht und Dunkeltieren). Aschoff, München. med. Wchnschr., 1922, **69**, 874.

No details are given.—J. K.

(THYROID) Radiotherapy in Graves' disease (La radiothérapie dans la maladie de Basedow). Barjon (F.), J. de méd. de Lyon, 1921; abst., Arch. méd. belges (Brux.), 1922, **75**, 208.

Radiotherapeutic treatment of Graves' disease is beginning to be used in the practice of medicine. The results obtained justify its use while at the same time they confirm the toxic origin of the symptoms, due to an abnormal ("anarchic") secretion of the thyroid gland. Four very different observations show the rapid action of irradiation upon the toxic symptoms, upon the general nutrition and upon hyperexcitation of the nerves. The action is constant and progressive upon tachycardia, but slower and less apparent upon exophthalmic goiter and tremor. This treatment is especially adapted to the serious and hypertoxic forms with menacing "subasystolic" symptoms.—R. G. H.

(THYROID) Radiotherapy in the treatment of Basedow's disease (Traitement radiothérapique de la maladie de Basedow). Belot (J.), Bull. méd. (Par.), 1920, **34**, 1063-1066.

The author assumes that hyperthyroidism is the main factor in the etiology and symptomatology of Basedow's disease, and therefore concludes that the rational treatment of this affection must be a method which reduces and modifies the thyroid secretion. Since the thyroid cells are highly sensitive to x-rays and thyroid intoxication is lessened thereby, this would seem to be the therapy of choice; there is no scar produced and relapses are less frequent than after surgery. The early results of x-ray treatments are a reduction of

nervousness, improvement in sleep and in gastro-intestinal symptoms, and in improvement in weight, hyperidrosis, and general well being. The circulatory symptoms, subjective and objective, are ameliorated. The pulse rate descends to 80, but rarely to normal. The goiter itself does not respond so readily; its reduction in size occurs some time after circulatory improvement is evident. Exophthalmos persists to the last, and if pronounced, may never disappear. Irradiation must not be continued because of the persistence of goiter and exophthalmos, lest **myxedema** result. Penetrating rays properly filtered, the use of a standard Coolidge tube with a 22 cm. spark, filtered through 5 to 7 mm. of aluminum, are the essentials of technique. The thyroid region is divided into three segments, corresponding to the two lobes and a median region which includes the **thymus.** The two lateral lobes are treated; this is followed within 4 or 5 days by treatment of the median thyroid region, including the thymus, the dosage being approximately 4 H. units. This is repeated every 10 or 12 days upon each segment. Belot emphasizes the importance of individualization in treatment, as a standard technique may not correspond with the requirements of a given case. Properly employed technique need not even discolor the skin. The subcutaneous adhesions complained of by surgeons as due to x-ray therapy are really evidences of improvement of the disease. Cure may be assumed when for two years the general condition has been good with the pulse rate about 80. Of 45 patients treated by the author, 20% showed "partial improvement," 70% presented "distinct prolonged improvement," 5% were not improved, and 5% of patients abandoned treatment. In discussing the indication for x-ray therapy, Belot divides his patients into 4 groups. Group 1 comprises patients presenting clear-cut symptoms of the Graves-Basedow type. Radiotherapy is capable of curing 80% of these. Group 2 includes the **forme fruste** type in which radiotherapy produces very prompt results. Group 3 includes the so-called "Basedowides" of Stern, in which radiotherapy is still a measure under discussion. Group 4 embraces the so-called "secondary Basedow" or toxic adenomata which do not respond to radiotherapy, but should be operated upon.—I. B.

(THYROID) Transitory paralysis of the recurrent nerve after goiter operations (Les paralysies transitoires du récurrent après les operations pour goîtres). Bérard (L.), Lyon chirurg., 1922, **19,** 1; abst., Arch. méd. belges (Brux.), 1922, **75,** 433.

The pathogenic elements of transitory paralysis of the recurrent nerve occur in the following order of frequency. There are twitchings of the lower vascular pedicle and of the recurrent nerve in the act of dislocation without injury of the descending lobe of the goiter which has been called the delivery of the goiter. There may be lesion of the nerve, from careless ligation of the thyroid artery.

Finally, and more rarely, there are cicatricial contractions of the tissues at the level of the hemostatic sutures in the vicinity of the recurrent nerves, or the blocking of one or two nerve trunks on account of the serum exuded from the thyroid stump, or by a neighboring hemorrhage. Before deciding upon the transitory character of postoperative recurrent paralysis each stage of the convalescence should be controlled by laryngoscopic examination, since there have been a number of cases of paralysis caused by section of the nerve with a definite cadaveric position of the corresponding vocal cord which seems to be wounded spontaneously, although it is a matter simply of a vocal adaptation by a more pronounced displacement of the healthy cord toward the median line.—R. G. H.

(THYROID) Does metastatic goiter exist (Le goître métastatique existe-t-il)? Bérard & Dunet, Rev. de chir. (Par.), 1921, **59**, 521; abst., Arch. méd. belges (Brux.), 1922, **75**, 223.

The authors deny the existence of benign metastatic goiter, introduced into thyroid pathology by Conheim, who described as benign a tumor which Wollfler affirmed to be malignant. That erroneous notion persisted due to the publication of observations on benign goiter, although in the great majority of cases either there was no microscopic examination of the goiter itself or it was made in a very inadequate fashion. Metastatic goiter, so-called benign, is a malignant goiter and the thyroid gland does not escape the general laws which govern the development of tumors; malignant thyroid neoplasm alone gives origin to metastases. In the presence of a tumor which is usually osseous, the microscopic examination of which reveals the thyroid nature, it is immediately necessary to investigate the changes which the thyroid gland itself may show. The presence of a large goiter, or of even a simple adenomatous nucleus, clinically benign, is frequent. But while a secondary tumor exists the clinical absence of signs of malignancy do not permit affirmation of the benignity of the thyroid lesion. Histologic examination may settle the question if made in serial sections and upon the whole initial neoplasm. In this case the microscope sometimes shows truly microscopical points of neoplastic degeneration. The idea of benign metastatic goiter should be eliminated entirely from the list of benign thyroid tumors and should give place to the conception of latent thyroid metastatic cancer.—R. G. H.

The morbid anatomy of the THYROID in six cases of DIABETES mellitus (En undersoekning av Glandula thyreoidea i 6 fal lav Diabetes Mellitus). Bergstrand (H.), Hygiea (Stockholm), 1922, **84**, 481-493.

Bergstrand has examined the thyroid gland of six patients dying from diabetes mellitus. In three the glands were practically normal. In the others the alveoli were irregular in shape and size.

The colloid was markedly diminished throughout the glands. The cuboidal epithelium showed some desquamation. In addition two of the glands showed chronic interstitial thyroiditis.—D. J. G.

HYPOTHYROIDISM (Über Hypothyroidie). Bolten (G. C.), Deutsche Ztschr. f. Nervenh. (Leipz.), 1917, **57**, 119-159.

A discussion of the function of the thyroid gland with special reference to what the author considers to be a particular form of hypothyroidism described in 1899 by E. Hertoghe as "benign chronic hypothyreoidea," but which, according to Bolten, has received far less attention than it deserves. Eleven cases are given to illustrate the various symptoms, which are discussed in detail. He gives the following outline of the symptoms in the adult. There is the primary or direct syndrome, which includes simple hyposecretion or hypofermentation of the stomach and intestine (nervous dyspepsia); metabolic disturbances in the form of incomplete catabolism, hypoexcretion of certain salts and delayed metabolism (a form of gout, gouty diathesis, ischialgia, etc., general constitutional obesity, and Dercum's disease); and toxic symptoms, probably resulting from incomplete fermentation during intermediate stages of metabolism, such as genuine migraine (thyrogenic), genuine epilepsy (thyroparathyrogenic), nervous disturbances of neurasthenic type, psychic disturbances resembling mild dementia praecox, and climacteric disturbances. Then there is the secondary or indirect syndrome (hypotonus of the sympathetic nervous system), which includes trophic and circulatory disturbances of the skin, nails and subcutaneous tissue (form of Raynaud's disease, herpes gangraenosus, etc.); circumscribed edema of the skin, and diminished or increased regenerative power of the skin. Forty references are given.—A. T. R.

(THYROID) Prevention of sporadic simple goiter. Bram (I.), Internat. Clin. (Phila.), 1922, **2**, 109-114.

In this illustrated article, the author emphasizes the importance of the clinical differentiation between endemic and sporadic simple goiter through an analysis of etiological factors, with special reference to the presence or absence of geographical conditions. It is easy enough, in a non-goitrous district, to conclude that a given goiter is sporadic in nature. It is rather difficult and often impossible, to make the distinction in patients residing in goitrous districts, as to whether the thyroid enlargement is induced by geographical conditions or otherwise. The writer's clinical observations in a large series of cases indicate this discrimination to be a guide in prophylaxis and treatment. Endemic goiter, a condition resulting from a geographical deficiency of iodine, is successfully managed by iodine administration. Not so with sporadic goiter, the etiology of which is complicated, depending upon excessive demands for thyroid hormone by physiological and pathological conditions elsewhere

in the body; the organ, incapable of supplying this excess, must hypertrophy in efforts at adjustment. Prophylaxis of sporadic goiter consists in the prevention of tangible causes which are usually referable to the sexual apparatus, or to local or general infection. Prenatal care of the child by attention to the goitrous mother is suggested in the prevention of congenital goiter. The necessary dietetic and hygienic precautions, the avoidance of excessive physical and mental exertion, and complete rest in bed for two or three days during each menstrual period will often prevent the occurrence of goiter in susceptible individuals. Though iodine administration in endemic goiter is productive of satisfactory results, endeavors to prevent or treat sporadic goiter routinely with iodine yields only occasional success. In a percentage of instances, the goiter becomes larger and toxic symptoms are induced. The drug to be employed in sporadic simple goiter (when a drug is indicated), is thyroid extract, carefully administered. Though iodine is an essential ingredient in all potent thyroid products, it is iodine in its thyroid environment or thyroid in its iodine environment that is required when the thyroid apparatus is to be relieved of its surplus burden of function. Thyroid minus iodine is impotent; with iodine it is thyroid as we know it—a substance at once a blessing and a curse in therapeutics and in sporadic goiter, depending upon whether it is used or abused.

—Author's Abst.

The position of the THYROID gland in the endocrine system. Brown (W. L.), Brit. M. J. (Lond.), 1922, **1**, 85-88.

After calling attention to the development of endocrinology and the relation of the autonomic nervous system to the endocrine glands, Brown discusses at some length the various thyroid disturbances. He divides the hyperthyroid cases into three groups, viz., (1) nutritional, (2) toxic, (3) psychic. The author notes the marked influence of the dysfunctioning thyroid on carbohydrate metabolism. The cardiovascular complications of thyroid disease are briefly described. Brown suggests that the **parathyroids** work with the **pancreas** and antagonize the thyroid gland. He believes that the thyroid gland should be considered as the activator of the metabolism; it co-operates with the sympathetic system and through it plays an important part in internal and external defense; it mobilizes blood sugar and prevents its escape by raising the kidney threshold; it interacts with the **gonads**, especially during their retrogressive changes.—F. C. P.

HYPERTHYROIDISM in children before puberty. Report of case. Buford (R. K.), J. Am. M. Ass. (Chicago), 1922, **78**, 1533-1534.

The author finds only 18 cases of hyperthyroidism in children under twelve years of age in the literature of the past twenty years. Two have had surgical treatment. The author's patient was 6 years old, showed no improvement after tonsillectomy and medical care,

but was in perfect health one year after partial thyroidectomy.
—W. M. A.

The effect of THYROID feeding on rats on a vitamin-deficient diet. Cameron (A. T.) & Moore (A.), Tr. Roy. Soc. Canada, 1921, **15**, 29-36.

Experiments on pigeons yielded no definite conclusions. It was doubtful if the onset of a definite polyneuritis was accelerated. Decrease in growth-rate in young rats due to thyroid and to deficient diet is additive. No definite conclusions could be drawn as to the joint effect on organ hypertrophy. The thyroid does not enter into a resting condition, as is the case when thyroid is fed with a normal diet.—A. T. C.

Case of recurring THYROIDITIS without other disturbances. Carling (E. R.), Proc. Roy. Soc. Med. (Lond.), 1922, **15**, 30.

The patient was a girl of 7 suffering with an enlarged thyroid in which there were 4 especially hard masses. No other abnormality was detected, and the swelling of the gland subsided spontaneously. The condition recurred on 3 subsequent occasions, at 3 months' intervals. In each instance, spontaneous recovery occurred.—I. B.

Influence of THYROID and ADRENAL on growth (Influenze delle glandole tiroide e surrenale sull' accrescimento corporeo). Castaldi (L.), Sperimentale. Arch. di biol. (Firenze), 1922, **76**, 110-113.

From extensive histological and biometrical investigations Castaldi concludes that the adrenals play an important rôle in conditioning somatic development. The correlation coefficient was found higher for the cortex than the medulla of the gland, as regards body weight and as regards sexual development the medullary coefficient was least. Hormone factors conditioning both pre- and post-natal growth are involved in a highly complicated way. In the treatment of growth disorders, therefore, **pluriglandular** preparations, including adrenal cortex, should be used.—P. M. N.

THYROID operations in the treatment of exophthalmic goiter (Les opérations thyroïdiennes dans le traitement du goitre exophthalmique). Cauchoix (A.), Bull. méd. (Par.), 1920, **34**, 1060-1063.

In France, surgical intervention in Graves' disease is not considered until non-surgical means have been tried without avail, since medical treatment has yielded cure, even in advanced cases. Surgery is especially contra-indicated during the acute phase in the progress of the disease, when there are observed hyperlymphocytosis, high **basal metabolism**, exaggerated nervousness, cardiac dilatation, marked emaciation, vomiting and diarrhoea. Nonsurgical treatment, especially rest and a rigid hygienic and dietetic regime, should be re-

sorted to; later, the critical stage having been passed, the question of surgical intervention may be faced. In grave cases, or when associated with an enlarged thyroid and there is a hypertrophied thymus, x-ray treatment may be advised. This should not be continued if clearly evident results are not quickly obtained. X-ray treatment should not be continued for a long time in any event, as fibrosis of the gland may render operation more difficult, and in some instances, prolonged irradiation may completely destroy the thyroid, resulting in myxedema. When surgery is to be resorted to, due care must be given the matter of the preparation of the patient. These subjects are extremely impressionable, irritable, and sensitive. Each emotional tension exaggerates the syndrome, and each fear increases the intoxication of the patient and the risk of operation. The principles of Crile's method of anoci-association are advocated. The author concludes his article with a review of the common operative procedures pursued in representative American clinics.—I. B.

The cerebrum and THYROID function (Il cervello e la funzione tiroidea). Ceni (C.), Riv. sper. di freniat. (Reggio-Emilia), 1920, **44**, 243-286.

In tortoises removal of one cerebral hemisphere produces no apparent change in the thyroid, but in birds and also in a certain number of the dogs experimented upon a thyroid hypertrophy occurred as a result of the operation. It is suggested that, in general, vertebrates possess an inhibitory center for the thyroid in the forebrain.—Physiol. Abst., **6**, 326.

(THYROID) Factitious toxicity of previously simple goiter. Chapman (T. L.), Minnesota Med. (St. Paul), 1921, **4**, 148-151.

Chapman warns against the indiscriminate use of iodine in the treatment of goiter. The prevention and cure of adolescent and preadolescent types of goiter by iodine is an assured fact, but goiter persisting after adolescence, though apparently nontoxic, may contain the essentials of toxicity. This may be due to scattered, relatively small areas of hyperfunctioning tissue within the struma, usually of insufficient size and bulk to produce a toxicity sufficient to give rise to clinical symptoms of recognized type. It is also possible that the small excess of thyroid hormones thus formed is neutralized by the protective forces of the body. Iodine may cause symptomless goiters to become toxic, and already toxic goiters to become more toxic. Toxicity caused by iodine administration is therefore a danger to be remembered. These instances of factitious toxicity are cases of thyrotoxicosis. Lastly, Chapman states that iodine administration shortens the period from nontoxicity to toxicity of simple goiter. Generally, a female of 16 to 30, who had sought treatment to improve her cosmetic appearance and had been placed upon prolonged iodine treatment, appears in the clinic because of increasing symptoms, especially goiter, tachycardia, sweating hands, tremor, and

nervousness. Examination of these goiters proves them to be granular; the cellular elements are confined to small areas, which are typically hyperplastic, though the entire gland never presents the picture seen in true Graves' disease nor do the subjects show true exophthalmos.—I. B.

(THYROID) Medical treatment of exophthalmic goiter (Traitement médical du goitre exophthalmique). Coulaud (E.), Bull. méd. (Par.), 1920, **34**, 1066-1069.

There are three classes of substances employed by the internist in the treatment of exophthalmic goiter: (1) Those not including opotherapy; (2) opotherapy; (3) serums of thyroidectomized animals or thyrotoxic serums. Cases evidently of infectious origin are treated along etiological lines. Those following acute rheumatic fever are relieved by sodium salicylate. Cases of syphilitic origin respond to mercury and arsenic. Since the thyroid is rich in arsenic and iodine, these drugs, employed indiscriminately, are apt to produce symptoms similar to those observed when thyroid material is administered. Iodine holds little, if any, place in the treatment of this disease. Many drugs may be employed for the symptomatic treatment of the disease. For the thyroid enlargement, quinine, ergot, and calcium chloride are useful. For the insomnia and trembling, the usual nerve sedatives are useful. Cardiac symptoms are not overcome by digitalis unless in myocardial insufficiency. Ordinarily, tincture of strophanthus in doses of 8 to 10 drops daily is advocated. Hydrotherapy also is of value. In instances in which the thymus largely participates in the toxic process, opotherapy may be considered. Few cases are ameliorated by thyroid opotherapy; these, as pointed out by Gauthier de Charolles, consist mainly of "Basedowified" types of the disease and those cases tending toward **myxedema.** Thyroid opotherapy and iodine administration are alike in their tendency occasionally to relieve but usually to injure patients with exophthalmic goiter. **Thymus** opotherapy, too, has its advocates and its opponents. In the author's opinion, thymus gland has been of little, if any, use, and in many instances it is as harmful as thyroid extract. Since there is a direct relationship between the thyroid and the genital organs and since there are strong evidences of **ovarian** insufficiency in patients suffering with exophthalmic goiter, ovarian opotherapy would seem to be a rational procedure. A large number of instances of clinical improvement has been observed following ovarian opotherapy. while not an instance of an exaggeration of the syndrome has occurred under this treatment. By analogy, **testicular** opotherapy has been employed in men with asserted favorable results, but hardly comparable to the effects obtained in women through ovarian administration. **Pituitary** and **suprarenal** opotherapy have been employed for their vasoconstricting action. Experiments on rabbits with the last mentioned substances have resulted in a diminution of colloid in the thyroid. **Parathyroid**

opotherapy has been recommended, but not upon substantial grounds. Revilliet has recommended biliary opotherapy to slow the pulse, but favorable results are not yet forthcoming. In concluding his remarks upon opotherapy, Coulaud is of the opinion that this mode of treatment has not given the hoped for results in the treatment of exophthalmic goiter; cures have been extremely rare. The hypothesis that following a thyroidectomy there forms in the organism a secretion capable of neutralizing the thyroid substance has led to the use of various serums. The blood of the thyroidectomized dog or horse administered to a subject of exophthalmic goiter may improve the tremor, tachycardia, and exophthalmos. The blood of a myxedematous person is said to possess analogous properties. The desiccated blood of thyroidectomized animals has also been used. Moebius' serum is an example. Some prefer to use the milk of thyroidectomized goats. These substances, when observed to alleviate the syndrome, do so only during the time of their administration. On the other hand, they are capable of harm. Rogers and Beebe have reported good results from the use of thyrotoxic serum, but subsequently have concluded that treatment is of little, if any, value.—I. B.

(THYROID) The influence of the diet during the war on Graves' disease (Einwirkung der Kriegskost auf die Basedowsche Krankheit). Curschmann (H.), Klin. Wchnschr. (Berl.), 1922, **1**, 1296-1298.

It is certain that underfeeding influences the thyroid. Oberndorfer found at post-mortem examination in all cases of "Hungeroedem" an atrophic thyroid. During the war Curschmann observed a largely increased number of patients with hypothyroidism and with classical myxedema. Meat, fat and, in general, a diet very rich in calories stimulates the thyroid and has a bad influence upon the symptoms not only in **diabetes**, but also in Graves' disease. During the war the number of patients with Graves' disease was exceedingly diminished.—J. K.

(THYROID) Malformation deformities of the neck; congenital cysts and fistulae (Deformità del collo per malformazioni embrionali. Cisti e fistole congenite). De Gaetona (L.), Arch. ital. di chir., 1921, **4**, 265; abst., Med. Sc. (Lond.), 1922, **6**, 29.

The article includes a discussion of thyroid, **parathyroid** and **thymus** tumors. It is of technical interest to surgeons.—R. G. H.

(THYROID) The value to the surgeon of the basal metabolic rate in toxic goitre. Else (J. E.), Northwest Med. (Seattle), 1922, **21**, 108-116.

The basal metabolic rate is an indispensable index of the activity of the thyroid gland. An increase in the secretion of thyroxin

is followed by an early rise in the rate, usually before the clinical symptoms are manifest. The height of the rate is not as important as the change in the rate, whether rapidly rising, stationary or falling. Frequent determinations are advisable. A normal or subnormal rate after an attack of thyrotoxicosis, accompanied by symptoms of the disease is indicative of permanent injury. Such symptoms may persist for life, even though there is no longer an excessive secretion of thyroxin. The prognosis is always guarded with a rising rate. The type of treatment, whether medical, surgical, or both, depends in part on the height of the rate and whether it is rising or falling. The type of operation, whether ligation of one or more arteries or single or double lobectomy is influenced in the same way.—H. L.

(THYROID) Riedel's sclerotic goiter (Riedelsche eisenharte Struma). Erkes, Klin. Wchnschr. (Berl.), 1922, **1**, 1128.

In this case, the goiter had shown inflammation. No other details are given.—J. K.

(THYROID) Riedel's sclerotic goiter (Riedelsche eisenharte zione gozzo-cretinica ereditaria). Ferrara (M.), Medicina nuova (Roma), 1920, **11**, 182-191.

During the war Ferrara, who was stationed in the Sabbia valley, had opportunity to observe a group of young men manifesting endemic hypothyroid disorders. The family history was determined in one instance. Of the parents and offspring, none was healthy. One daughter was most normal somatically, but an imbecile. Five sons showed varying degrees of **goiter, myxedema, dwarfism, mutism** or **mental retardation,** singly or in combination. The author comments on the fact that parents from an endemic goiter region may give birth to normal offspring if they remove to a more salubrious place, whereas previously healthy immigrants to a goiter region may have cretinous offspring; hence some local noxious influence must be postulated.—P. M. N.

(THYROID, GONADS) The influence of some endocrine glands on the course of experimental tuberculosis in the guinea pig (Contributo allo studio dell' azione di alcune glandole endocrine sul decorso della tubercolosi sperimentale nella cavia). Ferrata (A.), Folia med. (Napoli), 1922, **8**, 65-67.

Ferrata has studied the effects of the transplantation of gonads and thyroid on the course of experimental tuberculosis in the guinea pig. He concludes that subjects lacking the thyroid live a few days longer than the controls, while castration results in still longer survival unless the infection invade the thyroid. In castrated females, tuberculosis manifests itself as in the controls, but in a short time

they recover, increase in weight, and live a long time (ten months in the series reported).—P. M. N.

Anomalies of THYROID function in their bearing upon pregnancy (Des anomalies de la fonction thyroïdienne dans leurs rapports avec gestation). Fruhinsholz (A.) & Parisot (J.), Rev. franç. de gynec. et d'obst. (Par.), 1921, **16**, 603-605.

The subject is considered under two chief heads, the experimental and the clinical. The enlargement of the gland seen in pregnant animals is not merely hypertrophy, but also actual structural modification, characterized by rarefaction of the connective tissue and hyperemia. The mechanism of these changes is uncertain, but may possibly be sought in specific substances secreted by the unimplanted ovum and the foetal placenta. Thyroidectomy in early life prevents the development of the genital tract, the **uterus** and **ovaries** remaining infantile; in adult life it interferes with fecundation; in the pregnant woman it frequently causes abortion, premature labor, or stillbirth; it may also cause such special complications as **tetany**. On the other hand, with regard to the effect of gestation, labor or lactation upon the hypothyroid organism, several possibilities are mentioned: (1) no effect; (2) accentuation of the hypothyroidism; (3) tetany; (4) appearance of symptoms in subsequent pregnancies, even though they had not manifested themselves formerly; (5) mitigation of unpleasant symptoms, in certain cases, by injections of thyroid extract. Hyperthyroidism during pregnancy may be mild or it may assume the type of the characteristic Graves-Basedow syndrome. It seems that pregnancy evokes a compensatory hyperthyroidism, especially marked in the second half, and this may become pathologic. Hyperthyroidism is unfavorable to fecundation, but it often shows improvement during pregnancy. Hyperthyroidism may be ameliorated, aggravated or not influenced by gestation.—E. N.

The value of basal metabolic rate determination and the epinephrin test in the diagnosis and treatment of THYROID disorders. Goetsch (E.). Long Island M. J., 1922, 154; abst., J. Radiol. (Omaha), 1922, **3**, 298. (See Endocrin., 1922, **6**, 59-72.)

The writer studied approximately 800 patients suffering from disorders of the thyroid gland. All cases were carefully verified by histological study of operative material, and as a result the writer's clinical test for hyperthyroidism was evolved. In exophthalmic goiter (test usually unnecessary) the epinephrin reaction the writer found to be uniformly positive and parallel with the severity of the symptoms. In colloid goiter without symptoms of hyperthyroidism the reaction is negative. In active adenoma with clinical symptoms of hyperthyroidism the reaction is positive. In obscure cases presenting a hyperthyroid syndrome a positive epinephrin test has often

led the writer to advise operation at which adenomata, too small to be seen or palpated, have often been found and their removal has led to striking benefits. Patients with diffuse adenomatosis are often mistakenly thought to have tuberculosis, neurasthenia, psychoneurosis, effort syndrome, etc.; the metabolic rate is not increased in these cases and they are therefore overlooked. A positive reaction to the epinephrin test led to operation in 15 such cases with considerable consequent success. The epinephrin test is also a guide to the amount of thyroid extract administered in cases of hyperthyroidism, **myxedema** and **cretinism.** As a guide to differential diagnosis in tuberculosis, psychasthenia, psychoneurosis, hysteria, neurasthenia, dementia precox, melancholia, alcoholism, tabagism, **acromegaly** and arteriosclerosis as well as in some other disease, the test is of great value as essentially negative results are given. The writer does not hold that the test is absolutely pathognomic of hyperthyroid states—there are a few states which give a more or less typical reaction, but careful history and physical examination clears up such cases. The test is practically always confirmatory, in some other cases diagnostic and in other suggestive. The test is readily understood, performed and interpreted, having an advantage here over the basal metabolic rate test. In mild and latent cases of hyperthyroidism it is more sensitive than the basal metabolic rate test, though this latter is of distinct advantage in early diagnosis of hyperthyroidism and is a very useful guide to the form of therapy demanded by the case in hand, and also functions usefully as a check during treatment. The faulty technique and interpretation of this test are briefly dwelt upon.—R. G. H.

(THYROID) The pathology, diagnosis and surgical treatment of GOITER. Goetsch (E.), Northwest Med. (Seattle), 1922, **21**, 97-104.

Attention is specially directed to the pathologic origin from the alveolar epithelium of colloid goiter, puberty hyperplasia (adolescent goiter) and exophthalmic goiter (Graves' disease), and the nontoxic and toxic adenomata which arise from the fetal or interstitial cells. Large adenomas not infrequently degenerate from a solid into a cystic state and thus spontaneously cure the hyperthyroidism. Goetsch supports the purely surgical treatment of the adenomatous goiter, not having found any improvement from medical, x-ray or radium treatments. He grants a place to these measures where the abnormality consists of alveolar hyperplasia. Diffuse adenomatosis is described as the precise opposite, pathologically, of exophthalmic goiter, the former being a diffuse hyperplasia of the interstitial cells, whereas the latter is a diffuse hyperplasia of the acinar or alveolar cells. Goetsch warns against the expectant treatment of the adolescent goiter girl, strongly advocating surgery both as a curative and prophylactic measure. (Not all thyroid authorities will agree with this attitude.) The value of **basal metabolism** esti-

mates and the author's epinephrin test in the diagnosis of hyperthyroidism is fully expounded. Goetsch being convinced of the absolute reliability of his test believes it preferable to the basal metabolism test, because it is simple, less expensive, and less subject to technical error. The author believes in rest, low protein diet and removal of foci of infection, but does not believe that infectious foci ever cause frank hyperthyroidism. Their removal improves the general health of the patient which is of course advisable.—H. L.

The incidence of syphilis in HYPOTHYROIDISM and myxedema in children. Gordon (M. B.), N. York M. J. [etc.], 1922, **115**, 350-252.

This study is based upon the examination of the Wassermann and luetin reactions in 42 children suffering from some form of hypothyroidism in an attempt to evaluate the importance of syphilis as an etiological factor in the production of these diseases. There were 20 males and 22 females, the ages ranging from 18 months to 10 years. Two were positive to both Wassermann and luetin; 2 were positive to luetin; one was positive to Wassermann. There were 37 negative tests, making an incidence of 12 per cent. A search of the American literature is not conclusive as to the part syphilis plays in the causation of these diseases. The results obtained in this series indicate that syphilis is not of great etiological importance in the causation of either childhood myxedema or hypothyroidism in children. It is, however, possible for syphilis to attack the thyroid gland with the production of these conditions. The presence of a mental deficiency in 3 of the 5 positive cases is significant of the predilection of the spirocheta pallida for the brain and nervous system.—Author's Abst.

(THYROID) Graves' disease (Morbus Basedow). Gottlieb (K.), Wien. klin. Wchnschr., 1922, **35**, 553.

A girl of 11 years had an acute goiter, exophthalmos, tachycardia, perspiration, Stellway and Gräfe's symptoms. At this age Graves' disease is exceedingly rare.—J. K.

(THYROID) The disappearance of a goiter and improvement of cardiac insufficiency by irradiation of the ovaries (Beseitigung einer Struma und Heilung einer Herzinsuffizienz durch Röntgenbestrahlung der Ovarien. Ein Beiträg zur Fernwirkung der Röntgen-strahlen speziel auf endokrine Drüsen). Groedel (F. M.), Strahlentherapie (Berl. u. Wien.), 1920, **10**, 1047-1051; abst., J. de radiol. et d'électrol. (Par.), 1921, **5**, 42.

The existence of a correlation between the various endocrine glands and of an interdependence of their functions on activity has been discussed many times. In particular it has been tried to establish a connection between the function of the ovaries and that

of the thyroid. Graf also mentioned the appearance of an exophthalmic goiter following hysterectomy in one case and following destruction of the ovaries by radiotherapy in another. On the other hand, Mannaberg observed excellent results in ten patients suffering from Graves' disease and treated by radiotherapy by Kienböck, and Salzmann has published more recently (1919) an observation on a patient treated by radiotherapy for a fibroid in which a goiter of the size of two fists seemed to diminish very rapidly after existing 15 years, and the tachycardia and diarrhoea to disappear. It seems then that cessation of the ovarian activity might react on the function of the thyroid, more often as a moderator than an incentive, and that this point has not been discussed. Groedel's observation argues along the same lines. A patient examined and treated by him in 1908 for "cardiac insufficiency," with a goiter about the size of two fists, suffered in 1912 with such severe metrorrhagia and anemia that hysterectomy (it was a question of a small fibroid) was judged impossible and radiotherapy advised. Carried out by Groedel with complete success the menopause resulted in three series of sittings repeated after two months (the patient was 45 years old), at the same time that the goiter although large disappeared almost completely. and also all the cardiac symptoms. This "action at a distance" of the radiotherapy should be taken into consideration and would justify perhaps an attempt at systematic destruction of the ovaries by radiotherapy in the case of patients suffering from exophthalmic goiter and approaching the climacteric. Analogous attempts seemed equally justified before deciding upon surgical intervention, often dangerous, for the removal of large goiters. They would be the more interesting, seeing that in true goiter direct radiotherapy is generally followed by small enough results.

—Med. Sc., 1921, **5**, 93.

(THYROID) Graves' disease in the mountains (Basedowsche Krankheit in Gebirge). Guhr, München. med. Wchnschr., 1922, **69**, 837.

Mountain climate often leads to cure or at least marked improvement in Graves' disease.—J. K.

(THYROID) Goiter in infants (Kropf im Säuglingsalter). Hamburger (F.), München. med. Wchnschr., 1922, **69**, 819.

Goiter in infants is not rare in Steiermark. It is always a parenchymatous struma. When children with stridor show an increase in the symptom when the head is bent backwards there is probably a substernal goiter. Treatment consists in ointment with iodine and very small doses of NaI by mouth.—J. K.

Differentiation of HYPERTHYROIDISM and of heart disease from neurasthenic states. Hamilton (B. E.) & Lahey (F. H.), J. Am. M. Ass. (Chicago), 1922, **78**, 1793-1796.

A discussion of differential diagnosis, particularly by careful history taking and physical examination. Basal metabolic rate determination is considered of value in diagnosing hyperthyroidism, while the Goetsch adrenalin test is not.—W. M. A.

A case of THYROAPLASIA with reference to certain ENDOCRINE ORGANS [Ein Fall von Thyreoaplasia (dystropischer Thyreohypoplasie) unter Berücksichtigung gewisser der innersekretorischen und lymphoiden Organe. Abteilung I. Die innersekretorischen Organe]. Hammar (J. A.) & Hellman (T. J.), Ztschr. f. ang. Anat. [etc.] (Berl.), 1920, **5**, 218-267.

Hammar here describes the anatomical condition of **parathyroids, thymus, pancreas** and **suprarenals** and **ovaries** in a child a little over 4 years old with a rudimentary thyroid gland (2x2.5x2.5 mm.), situated near the foramen coecum. (The second part of this contribution is published by Hellman in Ztschr. f. Konstit., 1922. **8**, 336-360.) Histologically the thymus appeared to be in an early stage of accidental involution; the medullary portion, especially, was far below normal in volume; but the absolute volume of Hassall's corpuscles was within normal limits. There being no normal data to compare with his volumetric determinations on the other glands, no conclusions are drawn. The related literature is given.

—A. T. R.

A case of THYROAPLASIA with reference to certain lymphoid organs [Ein Fall von Thyreoaplasie (dystropischer Thyreohypoplasie) unter Berucksichtigung gewisser der innersekretorischen und lymphoiden Organe. Abteilung II. Die lymphoiden Organe]. Hammar (J. A.) & Hellman (T. J.), Ztschr. f. Konstit. (Berl.), 1922, **8**, 336-360.

This is the second part of a joint paper (the first part having appeared in Ztschr. f. ang. Anat. u. Konstit., 1920, **5**, 264). Hellman gives the detailed quantitative results of a determination by a new method of the amount of lymphoid tissue found in the intestines, mesentery and spleen of a 4 yr. 3 mo. old girl with only a small bit of thyroid tissue measuring 2x2.5x2.5 mm. In comparison with a single normal case which the author worked up, it appears that the lymphoid tissue in this case of thyroaplasia was below normal; but for want of comparable control data no conclusions are drawn.

—A. T. R.

(THYROID) Treatment of goiter with faradic current (Faradische Strumabehandlung). Hase (H.), Ztschr. f. phys. u. diätet. Therap. (Leipzig), 1921, **25**, 29-31.

Hase has for several months employed the galvanic current on goiter patients. The quartz rays were also tried. Results were generally unsatisfactory because patients discontinued treatment, owing to the slowness of improvement. Failure of these efforts led

the author to a careful trial of the faradic current. At first, patients with severe Basedow's disease were not accepted, but only those with vascular goiter possessing general Basedowian tendencies. Surprisingly good results were obtained in 8 patients; there was improvement in subjective symptoms and reduction in size of the goiter after six treatments. Thus encouraged, treatment of frankly outspoken cases of Basedow's disease was tried. These also soon began to show favorable changes; the tachycardia, sweating and irritability were improved, but the exophthalmos remained unchanged. There was striking improvement in a case of cystic goiter of several years' duration. A large number of adenomata were apparently influenced to the extent of becoming softer and smaller. Hase thus summarizes his results of the effects of the faradic current: The best results were obtained in vascular goiters; adenomata were more resistent to the faradic current, but showed a tendency to become softer, and in one case there was a disappearance of the pressure symptoms; the faradic current was without results in the retrosternal goiters and in the serious cases of Basedow's disease.—I. B.

(THYROID) X-ray treatment of Graves' disease (Röntgenbehandlung der Basedowschen Krankheit). Haudek (M.) & Kriser (A.), Klin. Wchnschr. (Berl.), 1922, **1**, 271-276.

The authors are quite certain that the x-ray is an excellent method of treatment for Graves' disease. It should be discontinued only when the pulse has become quite stable. The nervous symptoms generally disappear first, then the cardio-vascular symptoms, the diarrhea, the tremor and the perspiration. Often the **goiter** and the exophthalmos remain unaltered, but there are no other symptoms. Recurrence is not more frequent than after surgical treatment and the mortality is practically nihil. Adhesions are formed only when the x-ray treatment is not carried out in a systematic way. In formes frustes, even in heart neurosis, a good effect may be obtained by x-ray treatment of the thyroid. In Graves' disease it is necessary to expose the **thymus** also to x-rays. The authors believe that no patient with Graves' disease should be operated upon before an energetic x-ray treatment has been tried.—J. K.

HYPERTHYREOSEN. Hellwig (A.), Deutsche med. Wchnschr. (Berl.), 1922, **48**, 420-422.

Sudeck, in one of his studies on the surgical treatment of **Graves' disease,** makes the following classification. There is the classical Graves' disease, which is nearly always acute. Then he gives thyroidism, which is chronic and is a real hyperthyroidism. The symptoms in this form closely resemble those after administration of large doses of thyroid. Lastly, status neuropathicus is mentioned. Most of the so-called formes frustes belong to this class. Operation in these cases is never successful. Hellwig criticises this

scheme, however. He does not believe that there is so great a difference between classical Graves' disease and thyroidism. Sudeck (and Chvostek) think that tremor, loss of weight, irregularity of the pulse and eyelid symptoms are typical of thyroidism, but they are also typical of Graves' disease. The blood picture, the adrenalin proofs and the metabolism are the same in both forms. The author examined the histological picture of a large number of goiters and found a marked parallelism between this picture and the intensity of the symptoms. He agrees with the old unitarian view of Möbius that there is no great difference between all the forms of goiter. All are forms of hyperthyroidism. There are light and serious cases. The serious cases are those with symptoms of Graves' disease. According to Hellwig, Sudeck has proved that the serious forms of Graves' disease also also simple hyperthyroidism. This is proved by the fact that Sudeck was able to cure 5 very serious cases by complete removal of the thyroid. (See Janney, Endocrin., **6**, Nos. 5, 6.)

—J. K.

(THYROID) Surgical treatment of goiter (A propos du traitement chirurgical des goitres). Helsmoortel, Scalpel (Brux.), 1922, **75**, 625-528.

Of technical surgical interest. The literature quoted seems to indicate that only in France are goiters operated upon.—J. K.

(THYROID) The pathogenesis of exophthalmic goitre (Undersoekelser over Mb. Basedowiis patogenese). Holst (J.), Norsk. Mag. f. Lægevidensk. (Kristiania), 1922, **83**, 523-538.

The author has made serial sections of the thyroid tissue removed by operation, in a number of cases of early exophthalmic goitre and found islands of proliferating thyroid epithelium separated by normal tissue. He therefore concludes that even the diffuse proliferation found in advanced hyperthyroidism of this kind begins like the toxic adenomas as multiple tumor formation. Hence he believes the hyperthyroidism found is primarily due to the histological changes noted.—D. J. G.

(THYROID) Treatment of goiter. Hoag (C. L.), Calif. State J. M. (San Fran.), 1922, **20**, 6-8.

In treatment of goiter the pendulum has swung from medicine to surgery, and now over toward radiotherapy. The author makes the criticism that much of the treatment is carried on in a perfunctory way, without proper choice of cases and without a knowledge of the general principles essential to intelligent choice of therapeutic measures. Too many who have little experience even in general therapy are giving treatment for this malady. Diagnosis of thyroid disease is only the first step—it is just as necessary to recognize clearly the various forms of thyroid enlargement as to distinguish between different forms of intestinal parasites. For practical

purposes the following classification meets all requirements: (1) atoxic, (a) simple hypertrophy, adolescent goiter, (b) colloid, calcified or cystic, (c) simple adenoma; (2) toxic, (a) toxic adenoma, (b) hyperplastic (exophthalmic); (3) malignant, (a) carcinoma, (b) sarcoma, etc. In well developed cases it is easy to determine the classification of the goiter, but many border line cases give only mild symptoms and a large goiter may be deficient in thyroid secretion while a barely perceptible gland often is producing an extensive degree of hyperthyroidism. Since the thyroid secretion seems to be the principal regulator of the metabolic processes of the body an accurate estimate of its activity is secured by determining the **basal metabolism** in goiter patients. Many diseases influence the metabolic rate, but the influence of goiter is most striking. In the Crile and Mayo clinics radical operation is not done in toxic cases until the basal metabolism is less than plus 50%. Medical treatment, ligation of the superior thyroid arteries and x-ray are used until this point is reached, and even then the time of the operation must be determined by the phase for each indicated. The author believes x-ray or radium thrapy is indicated in simple hyperplasia and hyperplastic goiters only, and contra-indicated in colloid, cystic, nodular and adenomatous types. Treatment of goiter is essentially surgical, medical treatment. Roentgenotherapy and radiotherapy are sometimes curative and are often helpful in decreasing thyroid activity and in preparing the patient for operation.—J. Radiol., **3**, 117.

(THYROID) Technic of operation for goiter to improve postoperative cosmetics. Hunt (J.), Northwest Med. (Seattle), 1922, **21**, 104-107.

Before the patient enters the hospital, the head is flexed half way to the chest, and with a 15 per cent sliver nitrate solution on the butt of a straight needle, dots are placed at intervals along the natural crease of the neck. Incision is made later along the line of these black dots. The reader is advised to consult the article for further details of technique in operating, and closure of the wound—all contributing to immediate union, symmetry of the neck and almost invisible scar. The article is illustrated with several photographs.—H. L.

The THYROID. General surgery. Hubeny (M. J.), Pract. Med. Series, 1921, 226.

X-ray treatment of exophthalmic goiter is not to supercede surgery, but rather it is preferred in certain types because the percentage of cures is as great as following surgery. The earlier the cases are treated, the better the results. Favorable signs are lessening in nervous symptoms, lowering of the pulse rate, and disappearance or improvement in exophthalmos. The goiter might or might not decrease in size. In ambulatory cases there is no inter-

ference with the daily occupation. In marked thyrotoxic cases it is essential to regulate diet, to provide for mental and physical rest. Focal infections should be removed and special attention paid to the teeth. Some of the undesirable and dangerous possibilities were hypothyroidism, telangiectasis, and atrophy of the regions treated. Telangiectasis is more liable to occur in young women, and also if the filtration is insufficient or if erythema is produced several times. In discussing this paper, A. J. Ochsner stated that fifteen years ago this treatment was suggested. Many cases improved, but none of them seemed to show permanent improvement. Now the case is different. The technique has been worked out, the physics is understood, and by giving attention to the **thymus** gland something definite can be done.—Abst., J. Radiol., **3**, 113.

HYPOTHYROIDISM and the vicious circle. Hurry (J. B.), Practitioner (Lond.), 1922, **103**, 283-294.

Cretinism, endemic goitre, myxedema and minor thyroid insufficiency are described with their resulting derangements of growth and function in almost all the systems of the body. The author then suggests that these very alterations and abnormalities in turn repercuss as it were on the diseased thyroid, further depressing its activity, thus producing a vicious circle.—H. L.

(THYROID) Report of radium cases of head and neck. Jones (A. C.), Northwest Med. (Seattle), 1922, **21**, 140-143.

The author treated four cases of **goitre** with radium. A brief note is given of one woman aged 37, pulse 160, **basal metabolism** 146 plus, who was treated with 50 mg. of radium for two hours, screened with 1 inch of wood and 1 mm. of lead, over one area. The same screening with 75 mg. for three hours over two large areas was used. In three weeks basal metabolism had dropped to 41 plus. The same treatment was repeated. Two weeks later the pulse was 85 and basal metabolism plus 6. The remainder of the article deals with conditions treated by radium, such as cataract, cancer of lip, etc., and is not of endocrine interest.—H. L.

The control of x-ray therapy in HYPERTHYROIDISM by the basal metabolism test. Jones (H. M.), J. Radiol. (Omaha), 1922, **3**, 85-92.

The metabolism of the human organism may be defined as the sum total of the chemical changes going on in the cells of the body. To measure the rate of metabolism it is necessary to measure either the rate of heat production or the rate of chemical interchange above mentioned. This reduces to the task of measuring the oxygen intake. The final result is stated in terms of a plus or minus per cent of the patient's so-called normal rate. Muscular effort and food absorption have an effect upon the rate, therefore the test is preferably given

in the morning before breakfast, and with the patient lying down for from twenty to thirty minutes before the test is made. A concise table giving rates of metabolism for both sexes and for ages from six years to eighty has been compiled by Aub and DuBois. Any deviation of ten per cent from the normal rate is the basis of diagnosis for some twelve to fifteen pathological conditions of which there may be combinations. The test is used only for diagnosis of thyroid and **pituitary** abnormalities because the diagnosis for other conditions in which it might apply is more easily made by other means. It must be kept in mind that in a suspected case of hyperthyroidism these other pathological conditions may be affecting the metabolic rate, and also that in the presence of symptoms suggesting some other pathological condition the basal metabolism test is the only means of recognizing the beginning of hyperthyroidism. **Froelich's syndrome** can often be distinguished only by means of the test. **Addison's disease** is often confused with **myxedema** and thyroid therapy controlled by metabolism determination will differentiate these. The test is most valuable in border line cases. As to its being an index to operation the Mayo brothers believe that a patient showing a metabolic rate of plus forty per cent with an upward rate is a more dangerous risk than one with a rate of plus sixty and a downward rate. Age, nutrition, condition of the heart and other factors must also be taken into consideration. The surgeons' objections are that much of the gland may be destroyed, thus causing hypothyroidism, also many patients show no response to the treatment and the delay is made at the expense of myocardium. The radiologist in reply objects to surgery on the same grounds. Personal opinion and wrong diagnosis at the outset is responsible for many false conclusions. Also irregularity of dosage and variations in technique have led to a multiplicity of opinion for and against roentgen ray in hyperthyroidism. The secretion of the thyroid is unquestionably diminished by x-ray treatment, and, following wrong diagnosis, havoc has sometimes been wrought. Too small or too large dosage likewise brings disaster. A more perfect dosage is yet to be developed. The advantages are summarized as follows: No fatalities, no scar, no interference with the patient's occupation, it is painless, and if it is unsuccessful an operation will be less difficult. Means and Aub believe that surgery should be employed only after roentgen rays and other methods have failed. Some one hundred or more investigators show that the roentgen rays have a curative effect on hyperthyroidism. The most important uses of roentgen ray in these cases are in treatment of those showing a minor degree of toxicity and reducing the toxicity in more severe cases previous to operation.—Abst., J. Radiol., **3**, 111.

(THYROID) Experimental transformation of an axolotl into an amblyostoma. Kolzov (N. K.), Bull. Inst. Exper. Biol. (Moscow), 1921, **1**, 68-72.

This was accomplished by feeding on thyroidin. Many details are given and much theorizing—e. g., he attributes the general emaciation of the population of Russia since 1917 in a great part to hyperthyroidism, provoked by nervous shocks.

—Physiol. Abst., 1922, **7**, 195.

The action of THYROIDECTOMY and castration upon the islets of Langerhans. Konevskaia (E. O.), Med. Sc. (Lond.), 1919, **3**, 286-291.

Five dogs showed, after thyroidectomy and castration, an increase in number and an enlargement of the islets as compared with normal dogs.—Physiol. Abst., 1922, **7**, 194.

(THYROID) Importance of basal metabolism determinations and the test of induced hyperglycemia in the diagnosis of Basedow's disease (Importance de la mésure du métabolisme basal et de l'épreuve d'hyperglycemie provoquée pour le diagnostic de la maladie de Basedow). Labbé (M.), Stévenin (H.) & Nepveux (F.), Bull. et mém. Soc. méd. des hôp. de Par., 1922, **46**, 902-911.

A review of personal observations confirming the results of the American workers.—F. S. H.

A review of a year's THYROID work. Lahey (F. H.), Boston M. & S. J., 1922, **186**, 562; abst., J. Radiol. (Omaha), 1922, **3**, 297-298.

The writer believes that many errors in thyroid treatment are made because of inadequate knowledge of the clinical classification of thyroid disease and ignorance of the indications for operation. So-called adolescent goiter with slight enlargement requires no treatment. Colloid adolescent goiter seen in goiter belts is a different type. There is necessarily a relation between tachycardia and enlargement when both are present. Tachycardia of thyroid origin does not exist without other signs of this disease. The two conditions may exist even with a moderate increase in the basal metabolic rate without hyperthyroidism being present. If hyperthyroidism is present tachycardia and increased basal metabolic rate will be present also, but goiter may exist without hyperthyroidism, and vice versa. Colloid goiters and cysts, when unsightly or intrathoracic or associated with hyperthyroidism, Lahey would operate upon, also upon the latter when they produce pressure. Adenomata he believes should be operated upon if they are producing secondary hyperthyroidism or if they present danger of malignancy, this latter being especially stressed. Hyperthyroidism has not occurred in this group (five hundred cases) without an increase in basal metabolism rate; operations undertaken upon patients with normal metabolisms will yield consistently poor results. It is a grave error to consider thyroid disease in terms of increased metabolism, and metabolism test can be of as much harm as good unless carefully weighed and

correlated with the history and clinical signs presented by the individual. Most hearts in hyperthyroidism show no signs, upon clinical examination, of heart damage, but a smaller class shows definite signs of this. The writer's attitude toward x-ray therapy is exceedingly skeptical. Experimental work tried out under his management and with his selection of cases and interpretation as to cure or relief at the Boston City Hospital, leads him to conclude that surgery is preferable. He states, however, that the cases have been limited in number, and that as a clinician and not a trained roentgenologist, he has had no check upon the dosage, but he immediately counters this statement by one asserting absolute confidence in the accuracy of the dosage employed by the roentgenologist in charge.
—R. G. H.

Multiple stage measures in the surgery of severe HYPERTHYROIDISM. Lahey (F. H.), J. Am. M. Ass. (Chicago), 1922, **78**, 1862-1865.

By the use of such methods the author reports a mortality of 1.17 per cent in 342 thyroid operations.—W. M. A.

Three cases of HYPOTHYROIDISM. Law (W. F.), Tr. Roy. Acad. Med. Ireland (Dubl.); abst., Irish J. M. Sc. (Dubl.), 1922, **5** s., 142.

The first case was that of a woman, aged 60. The most striking features were hemorrhage from the bowel, and scantiness of the eyebrows in the outer third. The patient was also getting stouter and had a subnormal temperature. In the second case (a woman of 30) the patient complained of an almost constant feeling of chilliness with attacks of migraine. The attacks of migraine stopped during pregnancy and lactation, and then recurred. In the third case (a man, aged 29) there were slight neuralgic pains, scantiness of the outer third of the eyebrows, loss of energy and increase in weight. All three cases recovered completely on treatment with thyroid extract.—Quoted.

THYROID medication and hypotrophic infants (Médication thyroidienne et nourrissons hypotrophiques). Lesné, Bull. gén. de thérap. [etc.] (Par.), 1922, **173**, 271-272.

Lesné uses pluriglandular as well as thyroid therapy in disturbances of growth in infants. He gives daily for 10 days 0.02 gm. each of thyroid, **hypophysis** and **adrenal** powder and repeats after an interval of 10 days.—F. S. H.

Methods of estimating the activity and intelligence of normal and THYROIDECTOMIZED sheep. Liddell (H. S.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1922, **19**, 343-344.

Of technical interest.—R. G. H.

The effect of THYROID feeding on the bone marrow of rabbits. Lim (R. K. S.), Sarkar (B. B.) & Brown (Jane P. H. G.), J. Path. & Bactriol. (Cambridge), 1922, **25**, 228-246.

This investigation "is an attempt at a detailed cytological examination of the bone marrow, in an endeavor to determine the part played by it in the causation of the variable changes in the circulating blood corpuscles after thyroid feeding." Twenty rabbits were given daily doses of the desiccated thyroid powder of the British Pharmacopoeia. The conditions of the experiments were the same for all animals, as to time of feeding, time of taking blood counts, etc. For enumerating the marrow cells, marrow from the shaft and epiphyses of the femur was fixed in various fluids imbedded in paraffin, and cut in sections 5 microns thick. The most useful stains were found to be "the Romanowsky combinations, especially alcoholic eosin and methylene blue, and Giemsa." A number of squares, each 2 by 2 mm. were ruled on a cover glass and this was inserted in the eye piece of the microscope. By adjusting the tube length, using the oil immersion lens and a stage micrometer, the microscope was set so that each square represented an area of 0.0025 sq. mm. A minimum of 500 cells was counted, and from this the percentage of each type of marrow cell was determined. The bone marrow of young rabbits was found to differ from that of adults in containing fewer cells, and in exhibiting a higher percentage of polymorphonuclears than of small mononuclears. Thyroid feeding invariably caused an increase in the percentage of polymorphonuclears and a diminution of the small mononuclears, which is most marked in young individuals. In older animals and on continuing the treatment, the percentage of polymorphonuclears in the marrow falls and may become subnormal, while the percentage of mononuclears recovers and may be above normal. Daily doses of 0.25 to 0.5 gram per kilo of thyroid increase the total number of marrow cells, but larger doses may not do so; the qualitative changes, however, are always similar. Blood counts, red slightly and white more distinctly, are raised in young rabbits only; no changes occur in older animals except after prolonged feeding when a slight fall may occur. The differential count shows a marked relative polymorphonuclear increase in the young, and transitory and less marked increase in adult rabbits. The mononuclear percentage shows a fall when the polymorphonuclear percentage rises, but it does not show any rise above the normal even after prolonged feeding. These changes are not so constant in animals given heavy doses (i. e., more than 0.6 gm. per kilo), of thyroid. As to the significance of these findings, it is suggested (a) that the bone marrow is stimulated to activity under the conditions of these experiments, resulting in the increased production of polymorphonuclears and small mononuclears, according to the age of the animal. The mononuclears, however, do not reach the circulation as

such, since there is never any obvious increase in the number of blood mononuclears after prolonged thyroid feeding. They must therefore undergo development into another type, namely, erythroblasts and eventually erythrocytes. (b) That increased production in the marrow should lead to an increase of the corpuscles in the circulation. This is not evident from the blood counts, but may be masked by some such factors as an increased destruction of cells, an increased blood volume, circulatory changes, etc. (c) That the marrow mononuclears are not responsible for the supply of mononuclears to the blood stream and therefore do not function as lymphocytes.—J. P. S.

(THYROID) Fats in relation to the genesis of goiter. McCarrison (R.), Brit. M. J. (Lond.), 1922, **i**, 178-181.

This author first summarizes a previously reported (Indian J. M. Research, Jan. 1920) experimental study of the thyroid weights in groups of pigeons fed with fat in form of butter, where he found goiter present in 65% of the birds fed with butter fat, and that the histology of these thyroids resembled that found in the thyroids from cases of Graves' disease. The present paper deals with a similar study in which pigeons and tadpoles were used. The hygienic surroundings were not as perfect as in the previous experiments and the work was done in a region (Oxford, Eng.) known to be in a goiter belt. Twenty-eight birds were used and the feedings consisted of 50 gms. of mixed grains, to which was added 1.6 cc. of oleic acid for 7 birds, 4 gms. of butter fat to the food of 7 others, and 1 dram of cod-liver oil (containing 0.002% iodine) to the ration of 7 others, while the remaining birds were fed on the mixed grains. At the end of 143-144 days the pigeons were killed and the average weights of the thyroid glands noted. The glands from the controls averaged 537 mgs., those fed with butter fat 675 mgs., those with oleic acid 909 mgs., those with cod-liver oil 93 mgs. McCarrison calls attention to the marked difference in the weight of the thyroids from pigeons fed on cod-liver oil. To determine the relation of fat excess and iodine intake, groups (50) of tadpoles were fed with a flour caseinogen mixture to which was added butter fat, oleic acid, cod-liver oil, or varying amounts of iodine. An excess of fats caused remarkable retardation in the growth of the tadpoles. The iodine in amounts of 0.5 to 1 gm. per gram of food tended to prevent the retardation of growth induced by the butter fat and oleic acid, but not that caused by the cod-liver oil. The retardation of growth induced by the fats was associated with a delayed development of the thyroid gland. McCarrison states that he believes that the composition of food has an important bearing on the genesis of goiter, that food must be considered both in its relation to its content of available iodine and in its relation to its content of fats, that variations in the histologic types of goiter may result from the variations in the composition of goiter inducing foods.—F. C. P.

(THYROID) The rôle played by the physician and surgeon in the treatment of Graves' disease. McKay (W. J. S.), Med. J. Australia (Sydney), 1920, **ii**, 357-359.

A general discussion of therapeutic procedures.—R. G. H.

(THYROID) Roentgen ray treatment of toxic goiter. Means (J. H.) & Holmes (G. W.), Tr. Ass. Am. Physicians, May 2-4, 1922.

Of 44 cases of exophthalmic goiter, definite improvement was secured by roentgenotherapy in 28. Sixteen showed little or no improvement; eight of these patients later came to operation and were apparently cured. Of the 28 in which there was improvement, there were 13 who were apparently cured, and 15 who were improved but not rendered entirely free from hyperthyroidism. No patients seemed to be made worse by the treatment. Two patients improved but not cured were operated on later. One of these died after operation. Of the 12 toxic adenoma cases treated by roentgen rays, all showed improvement and 5 patients were apparently cured. Two of the exophthalmic and one of the toxic adenoma cases developed **myxedema** during roentgen ray treatment, which was promptly relieved by thyroid administration, and in the two exophthalmic patients the depression was only temporary, as thyroid was later discontinued without a return of myxedema. In those cases of exophthalmic goiter which respond to roentgen rays there is a rapid fall in pulse (average from 115 to 89) and in basal metabolism (average from + 55 to + 21 per cent), and a corresponding gain in weight (average of 9 per cent) in the first 4 months of treatment, during which time they receive on an average 5 treatments. In some cases the curves come to a normal level; in others they do not. In the latter further roentgen ray treatment is not strikingly satisfactory except in the cases which show a definite relapse; in these a second course of treatment may act as did the first. We have as yet found no method of predicting which cases will respond to roentgen rays. The results in toxic adenoma are similar to those in exophthalmic goiter. In general, we feel that roentgen rays may cure certain cases, that it may improve others; that for this reason it has its place in the treatment of toxic goiter. If it does not secure good results in a few months, surgery should be employed. Some patients who are not cured by roentgen rays are rendered better operative risks. A combination of roentgen rays and surgery will sometimes accomplish more good than either form of treatment alone. To make a proper use of the roentgen rays in the management of toxic goiter, its limitations must be recognized and, when necessary, it should be combined intelligently with surgical procedures.

—J. Am. M. Ass., 1922, **79**, 67.

Cancer & opothérapie. Naamé, Gaz. d. hôp. (Par.), 1921, **94**, 170-172.

Two cases diagnosed as epithelioma showed recovery after taking bile, **thyroid** and **pancreatic** extract in combination. The author repudiates a suggestion that the neoplasms were syphilides that healed as a result of iodine (thyroid) medication.—R. G. H.

Effect of THYROID colloid on tubercle bacilli. Nathan (K.), Ztschr. f. Tuberk. (Leipz.), 1921, **34**, 390-391.

The rarity of thyroid gland tuberculosis may be due to an inhibitory action of its secretions, especially of the colloid of the gland. With this in mind the colloid was pressed out of thyroid gland substance and graded quantities of tubercle bacilli were mixed with it and exposed for from 4 to 24 hrs. at 37° and then injected into guinea pigs. The injected animals, however, showed no longer duration of life than the control animals.—Chem. Abst., **16**, 1617.

(THYROID) A case of goiter recurrence (Rezidiv von Basedow). Neupert, Klin. Wchnschr. (Berl.), 1922, **1**, 1232.

Some time after hemistrumectomy the other half of the thyroid became enlarged. The arteries were so strongly developed that the rest of the thyroid looked like an angioma arteriale racemosum.
—J. K.

(THYROID) Basedow syndrome and trophic edema (Syndrome de Basedow et trophoedeme). Parhon (C. J.) & Stocker (A.), Rev. neurol. (Par.), 1920, **27**, 1020-1031.

A female, single, aged 21, had had an onset of illness 2 years before, following a fright. There was a gradual development of Basedow's disease with palpitation, tachycardia, tremor, swelling of the thyroid, exophthalmos, headaches, irritability, nausea, vomiting, insomnia, dyspnoea, and weakness. Treatment was variegated, including bromides, iodides, arsenic, thyroid extract, antithyroidin, and 8 months' rest in bed, with but slight improvement in the general condition during the administration of arsenic. Edema beginning at the instep was observed. This soon extended upward, involving the entire lower limbs, and was attributed by the patient to the obesity which developed during the arsenical treatment. The infiltration of the lower limbs inhibited their power of locomotion and the usual actions of the day, such as getting off and on the bed, sitting down, etc., became extremely difficult, resembling the movements of a case of myopathy. There was no change in color or temperature of the skin and no pitting on pressure. The diagnosis of trophic edema complicating Basedow's disease was made. Such an association is rare; the author in perusing the literature could find but 25 such instances recorded. The article contains a valuable review of the subject of trophic edema and allied conditions, with causal theories advanced by the numerous authors mentioned in the bibliography.—I. B.

Organic reactions and THYROID extracts in disturbances of the thyroid function, "the thyroid sign" (Réactions organiques et extraits thyroidiens dans les troubles de la fonction thyroidienne, "le signe de la thyroide"). Parisot (J.) & Richard (G.), Bull. et mém. Soc. méd. des hôp. de Par., 1922, **46,** 806-810.

The authors studied the effects of thyroid extract injections on 72 persons distributed as follows: 17 Basedowians and patients with hyperthyroidism, 32 persons of normal gland function, and 12 persons presenting signs of hypothyroidism. The general observation is that a massive injection of 1 gm. of thyroid extract may produce modifications in the pulse, arterial tension and oculo-cardiac reflex. The pulse of the normal individuals is not changed beyond normal limits of variation by thyroid administration. Hyperthyroid cases respond by a slowing of from 10 to 30 beats, while hypothyroid cases of all types do not respond, or if at all, by a slight acceleration. The oculo-cardiac reflex is not significantly altered in normal persons subjected to injection of thyroid extract, while persons exhibiting hyperthyroidism show a slowed positive reaction and in those with hypothyroidism the reaction is reversed. In normal persons and those with hypothyroidism the injection of thyroid extract does not modify the maximum arterial tension, but raises the minimum for 10 or 15 minutes. In hyperthyroid cases, however, the minimum is not affected, but the maximum drops from 20 to 40 mm. These reactions were obtained from deproteinized extracts and are interpreted as vagal in origin. The "thyroid sign" is the response by hyperthyroid patients to the injection of thyroid extract.

—F. S. H.

(THYROID) Treatment of goiter (Traitement des goitres). Pauchet (V.), J. de méd. de Par., 1921, **40,** 81-84.

This is a review of the applied anatomy of the thyroid with respect to goiter, and of the operative technique advised by the author. The article is of no general endocrine interest, but may be found of service to the surgical technician.—I. B.

(THYROID) Differential diagnosis of diseases of the mediastinum. Phillips (J.), J. Am. M. Ass. (Chicago), 1922, **78,** 1355-1363.

Intrathoracic thyroid is considered among other tumors of the mediastinum for differential diagnosis and one case is reported in detail.—W. M. A.

(THYROID) Must the wound after strumectomy be closed or drained (Völliger Wundschlusz oder Wundschlusz mit Drainage nach Kropfoperationen)? Propping (K.), Zentralbl. f. Chir. (Leipz.), 1922, **49,** 829-830.

Of technical, surgical interest.—J. K.

(THYROID) Goiter prophylaxis in Bern (Kropfprophylaxe in der Stadt Bern). de Quervain & Lauener, Klin. Wchnschr. (Berl.), 1922, **1**, 344.

In Bern 73.2% of the children of 7 years have an enlarged thyroid; 34.7% have even a very large thyroid. Of the children of 15 years 93-94% have a palpable gland. Thus the so-called "school prophylaxis" is no prophylaxis but a real treatment. There are several different forms of prophylaxis in the schools in Switzerland, all of which bring good results. Iodine is put in open vessels in the school rooms or it is given as amulet to the children. Very small doses of iodine salts or of iodine containing fatty acids are given. It is theoretically not impossible that the number of cases of Graves' disease may slightly increase, since serious Graves' disease is especially seen in countries without endemic goiter.—J. K.

(THYROID) La coexistence de l'endémie goitreuse et du syndrome de Basedow dans un village des Hautes-Pryénées. Regnault (F.), Soc. de méd. de Par., April 14, 1922; abst., Presse méd. (Par.), 1922, **30**, 361.

Graves' disease in this village is often complicated by goiters brought about by pregnancy or excitement or by no appreciable cause at all.—R. G. H.

(THYROID) Quantitative studies on the action of thyroxin, dijodtyrosin, jodothyrin and jodthyreoglobulin (Quantitative Untersuchungen über die Wirkung von Thyroxin, Dijodtyrosin, Jodothyrin und Jodthyreo-globulin). Romeis (B.), Klin. Wchnschr. (Berl.), 1922, **1**, 1262.

The author studied the influence of these substances on the development of tadpoles. Thyroxin proved to be very powerful in producing a quickened development. Its action is the same in young or old tadpoles. Much more dijodtyrosin, however, is required to accelerate development in old than in young tadpoles. —J. K.

(THYROID) Basal metabolism of patients with Graves' disease after x-ray treatment (Respirations—Stoffwechselversuche an Röntgenbehandelten Basedow Kranken). Roth (N.), Wien. Arch. f. innere Med., 1922, **3**, 367-378.

The author reports 4 cases of classical Graves' disease and one case of formes frustes (exophthalmos, tremor, restlessness, Kocher's blood picture, but with normal metabolism and without alimentary glucosuria). In three cases of Graves' disease, especially in an acute case, the highly increased basal metabolism became normal and the complaints of the patients disappeared. In a fourth case x-ray treatment had no effect. In the formes frustes metabolism was normal and remained unaltered by treatment;

though the patient became more quiet after treatment, the other objective symptoms did not improve.—J. K.

(THYROID) Hyperthyroidism with use of Goetsch test and glucose tolerance determination in diagnosis. Rucks (W. W.), J. Oklahoma M. Ass. (Guthrie), 1921, **14**, 93.

Rucks reports a case in a married female of 27, in which the main features were nervousness, loss of weight, hyperidrosis, tachycardia, palpitation, dyspnoea, and disturbed sleep. The apparent duration of the illness was 18 months. Teeth and tonsils presented evidences of focal infection; the thyroid was enlarged, the heart sounds were snappy in nature, there was a tremor of the outstretched fingers and hyperactive reflexes. The patient's history revealed the fact that she had been given ten grains of sodium bromide t. i. d. by another physician for a long time. A diagnosis of hyperthyroidism was made, although some of the symptoms were attributed to the prolonged use of bromides. Treatment consisted in tonic and dietetic management, with the administration of sodium chloride as an antidote for chronic bromide poisoning. After a preliminary stay in the hospital the patient was sent home. Within 3 months she returned to the institution, when both the Goetsch adrenalin test and the glucose tolerance test proved positive. A subtotal resection of thyroid was advised.—I. B.

(THYROID) Prognosis in mental disease. Rutherford (H. R. C.), Tr. Roy. Acad. Med. Ireland, Sect. Med.; abst. Irish J. M. Sc. (Dublin), 1922, **5** s., 93-94.

For purposes of comparison, the author made a classification of states, instead of entities. He divided them into four types—depression, excitement, confusion and delusion. An analysis had been made of 157 recoveries. A depression state was present in 63 cases. The general recovery rate, as estimated upon the admissions, had worked out at 43.13%. Permanence of recovery was not to be found, as a rule, in mental disease, owing to the influence of heredity. Heredity was usually to be discerned in from 50% to 70% of admissions. This heredity he regarded as being purely of a hypothyroidal nature. He had come to this belief by the large number of patients, with an early psychopathic inheritance, who responded to thyroid treatment. Especially was this to be noticed in cases showing a family history of collateral heredity. The later hypothyroidal generations showed dementia praecox and imbecility, which conditions were accompanied by degenerative changes, or un development, and these the late administration of thyroid could not remove. He commented upon the influence of thyroid in the organism's growth, and suggested that the want of durability in degenerated tissues was due to deficient thyroid, so that when strain came the affected organ failed. Hypothyroidism only acted as a predisposing cause, but whenever the exciting cause of the mental

attack was a feeble one, the administration of thyroid would remove it. There was a marked association in both the insane and their relatives, of tuberculosis, asthma, and malignant disease. The author suggested that defective thyroidal secretions might act as an hereditary and predisposing cause in these diseases also. Infections of all sorts, especially intestinal, are very common in the insane, and he thought, due largely to the hypothyroid state. The thyroid, and occasionally, the **suprarenal**, were the only glands which had given him results.—Quoted.

The rôle of the THYROID gland in otolaryngology. Schatz (H. A.), Penn. M. J. (Harrisburg), 1922, **25**, 529-538.

The subject is considered under the following headings: hemorrhage, epistaxis; affections of the nose and asthma; the mouth and fauces; the tonsils and adenoids; headache and migraine; the voice and larynx; the ear and deaf-mutism; diagnosis; pathology; treatment, drugs, clinical studies. Twenty-four articles are collected in the bibliography and repeated references to them are made throughout the article. As the article itself is largely an abstract, it hardly lends itself to further condensation. An interesting discussion of this paper and those of Fridenberg and Zentmayer follows.—H. L.

The influence of the THYROID on metabolism with especial regard to heat regulation (Über den Einfluss der Schilddrüse auf den Stoffwechsel mit besonder Berucksichtigung des Wärmehaushalts). Schenk (P.), Arch. f. exper. Path. u. Pharmakol. (Berl.), 1922, **92**, 1-21.

The metabolism of a thyroidectomised rabbit differs greatly in starvation from that of a normal rabbit. While in the thyroidectomised animal the CO_2 output diminishes greatly, the oxygen intake diminishes much less, so that the author records a respiratory quotient at times less than 0.5. The urinary nitrogen is much less in the starving thyroidectomised animal, and consequently it lives much longer than does the starving normal. The intravenous injection of thyreoglandol (used as the active principle of the thyroid gland, though stated to be almost iodine-free) is claimed to produce a large rise of metabolism in the thyroidectomised animal, but not in the normal animal (a claim hardly borne out by the figures given). The influence of thyroid in heat regulation is demonstrated by the fact that a starving thyroidectomised animal cooled to 33° took 1 hour longer to return to normal than did a starving normal animal cooled to 36°. Finally, the serum of a cooled animal, rich, according to the author, in thyroid hormone, was without effect on a second normal animal until this second animal was thyroidectomised. The serum of the cooled animal injected into the second

then produced a large rise in metabolism. Serum taken from a cooled thyroidectomised animal was ineffective.

—Physiol. Abst., **7**, 256.

A case of congenital ATHYREOSIS (myxedema) with special regard to muscular alterations (Ueber einen Fall von Athyreosis congenita (Myxödem) und besonderer Berücksichtigung der dabei beobachteten Muskelveränderungen). Schultz (A.), Virchow's Arch. f. path. Anat. (etc.) (Berl.), 1921, **232**, 302-315.

A report of a case of congenital myxedema in a female child of 7 years. Thyroid medication, begun less than a month before death, which was due to broncho-pneumonia, resulted in "greater liveliness" and increased interest in her surroundings. At necropsy no trace of thyroid tissue could be found although there was a small cyst filled with clear fluid in the region of the right lobe of the thyroid. Three **parathyroids** were present and apparently normal on microscopic examination. The **thymus** was small, the differentiation between cortex and medulla indistinguishable, and Hassall's corpuscles were few in number and small. The **hypophysis, adrenals** and **pineal** gland showed nothing noteworthy. There were numerous large islands of Langerhans in the **pancreas.** The **ovaries** showed many well developed follicles. In the muscle of the tongue and of the thigh, Schultz found great variations in the width and a varicose distortion of the fibers. In some fibers there was herniation of the sarcoplasm. The striations were lost. In places there was a proliferation of the sarcolemma nuclei; in other places the nuclei were shrunken and pyknotic.—J. P. S.

(THYROID) Keratitis diffusa fetalis (ichthyosis congenita). Hess (J. H.) & Schultz (O. T.), Am. J. Dis. Child. (Chicago), 1921, **21**, 357-389.

Hess and Schultz report a case in a child one day old who died eight days later. Because of alterations which occur in the skin in conditions of loss of thyroid function, it would seem pertinent to consider the possibility of relationship of abnormality of thyroid function to keratitis diffusa fetalis. Absence of or failure of development of the thyroid has been noted by Winfield and by Moore and Warfield. In Wassmuth's case, the parents were high-grade cretins. In Moore and Warfield's case the **thymus** was atrophic and fibrous. In Hess and Schultz's case the thymus showed no striking deviation from normal, except richness in Hassall's corpuscles, but the thyroid gave definite morphological evidence of loss or absence of function. With the exception of four small and relatively insignificant areas, the thyroid was totally undifferentiated. It was composed of small cells without any follicular arrangement and with no formation of secretory material except in the small areas noted. In general, the abnormality of the thyroid in this case appeared to

be of the same nature as in the case noted by Moore and Warfield. The condition of the thyroid is striking and suggestive, but thyroid deficiency cannot be considered an essential factor in keratitis diffusa fetalis unless it occurs more frequently or more uniformly than the previous literature indicates. None of the other glands of internal secretion showed any deviation from the normal which might be held to have any relation to the general condition.

—M. B. G.

(THYROID) Treatment of Graves' disease (Behandlung der Basedowschen Krankheit). Schloessmann, Klin. Wchnschr. (Berl.), 1922, **1**, 243.

See Endocrin, 1922, **6**, 472.—J. K.

(THYROID) Certain actions at a distance produced by x-rays (Di talune azioni a distanza prodotte dei raggi X). Serena (M.), Radiol. med. (Torino), 1920, **7**, 203.

A study of the effects of small or medium doses of x-rays which produced distant changes when applied to certain glands, apparently through the medium of an action on the **internal secretions.** Cases are quoted to show how a series of small stimulative doses applied to the thyroid or **genital** glands led to correction of menstrual functions and the clearing up of psoriasis and other dermatoses. The author regrets that there is no clue as yet to the proper dose of rays to the thyroid for procuring restoration of normal menstruation.—Med. Sc., 1921, **3**, 476.

Activity of the THYROID gland and immunity processes (Sulla attività della ghiandola tiroide nel processo immunitario). Sestini (C.), Sperimentale. Arch. di biol. (Firenze), 1922, **76**, 79-86.

Sestini studied the histological and histochemical modifications of the thyroids in guinea pigs vaccinated with the Eberth bacilli. He observed hyperemia of the gland, increase of the colloidal substance and of the epithelial cell volume, turgid nuclei, cells rich in fuchsinophil granaules and, especially, augmented lipoid granules —in short, evidence of hyperfunction.—P. M. N.

THYROID The surgical treatment of exoptholmic goitre. Shawan (H. K.), Grace Hosp. Bull. (Detroit), 1921, **5**, 8-14.

With Plummer's classification as a basis, Shawan discusses hyperplastic and adenomatous goitre, stating that in mild or moderate stages, removal of all sources of infection and medical treatment should be tried, but advocating radical operative treatment in severe, or serious stages, as well as in cases of moderate toxicity not improved by rest. Crile's operative technique is followed. The author stresses the fact that adenomata are always surgical, and that clinical judgment must supplement laboratory tests of toxicity.

—C. R.

(THYROID) Goiter operation technique. Sloan (E. P.), Illinois M. J., 1921, **39**, 130-133.

The writer regards associated heart pathology as the only definite bar to removal of a diseased thyroid, and where auricular flutter or fibrillation are present, prefers gland injection, or ligation of the inferior thyroid arteries to ligation of the superior thyroids. The technique of local anesthesia thyroidectomy, which he now uses in all cases, is given in detail. Removal of the entire diseased portion, the whole gland if necessary, is urged, and surgery is advocated in all cases as reliable, prompt, and, under local anesthesia, comparatively safe.—C. R.

(THYROID) Case of exophthalmic goiter. Smith (E. B.), Proc. Roy. Soc. Med. (Lond.), 1922, **15**, 30.

This is the report of a girl, aged 13⅔ years, who was taken to a throat hospital on account of some difficulty in swallowing. In the course of time a definite diagnosis of exophthalmic goiter was made. The case is reported because of the infrequency with which the disease occurs in children.—I. B.

(THYROID) Technik der Strumektomie. Streissler, Klin. Wchnschr. (Berl.), 1922, **1**, 1128.

A few technical details are given.—J. K.

X-ray treatment of the THYROID (Bestrahlungen der Thyreoidea). Szegö, Deutsche med. Wchnschr. (Berl.), 1922, **48**, 888.

There is no marked reaction after injection of **adrenalin** after the thyroid has been exposed once or twice to x-rays.—J. K.

(THYROID) X-ray treatment of Basedow's disease. Trostler (I. S.), Am. Physician (Rahway, N. J.), 1921, **26**, 289-291.

The author, a roentgenologist, is opposed to the medical treatment of Basedow's disease on the grounds that only 20% of the patients are cured, and in these relapse is common. He is opposed to surgery because the operative risk is too great. He claims that x-ray treatment cures in 90% of the instances, and this without operative risk. The following are the reasons given for the superiority of x-ray therapy: it is harmless, and has helped and cured many; there is no operative risk; there is no fear of operation; there is greater likelihood of cure and less likelihood of recurrence; there is likelihood of earlier cure and shorter period of disability; and there is no scar. The author cities DaCosta and the Mayos as surgeons who submit their patients to x-ray therapy prior to operation. In Trostler's experience 4 to 8 full dosage treatments effect the cure. The **thymus** is also submitted to x-ray treatments in all cases. A note of warning is sounded in the interest of the cautious use of the x-ray, for an agency which is so potent for good is capable

of doing harm when improperly handled. (In this paper, the terms Basedow's disease and hyperthyroidism are used synonymously.)
—I. B.

HYPERTHYROIDISM, basal metabolism and radiotherapy. Van Allen (H. W.), J. Radiol. (Omaha), 1922, **3**, 83-85.

Hyperthyroidism is a much more common condition than is generally supposed, and in many cases no appreciable enlargement is present even when a plus result is given by the basal metabolism test. Many of these cases are diagnosed as neurasthenia or as disease of the heart muscle. Too much attention has been focused upon "characteristic symptoms" and too little upon the lesser symptoms of nervousness, unusual perspiration, staring eyes with almost entire absence of winking, mental irritability, and slight but gradual loss of weight. The patient may be almost invalidized and only obscure symptoms be present. It is in such cases that the basal metabolism test is invaluable. In treating these cases there is a proper dosage which must be observed or the result will be a failure. The author's technique is 3½ milliamperes, 15 minutes, 4½ mm. aluminum filter, 8½ in spark gap, 16 inch distance, 6 treatments on each side of the neck (12 treatments in all) given twice per week. This has been used for years with excellent results. Though a few cases have had to be re-treated, no case has had **myxoedema** and there have been no deaths. The author believes the basal metabolism test should be given in all cases where a diagnosis of hyperthyroidism is made and in all cases of obscure nervous or suppressed cardio-muscular disease. The test should be given while the patient is in a state of mental quietude and physical rest. The home or the laboratory is a better place than the hospital as a rule because a trip to the hospital is for most people a cause of at least some degree of excitement and nervous strain. After the first test no further one is required until at least a month after the last treatment has been given; the pulse is relied upon to indicate changes in the condition. Charts are shown to illustrate the accuracy of the pulse as an indication of the effect of treatment.—Abst., J. Radiol., **3**, 112.

(THYROID) The pathology of toxic and nontoxic adenomatous goiters. Wilson (L. B.), Tr. Ass. Am. Physicians, 1922; abst. J. Am. M. Ass. (Chicago), 1922, **78**, 1918-1919.

True exophthalmic goiter can be divided into three stages: (1) early stage, with moderate increase in **basal metabolism**, often moderate exophthalmos, moderate enlargement, moderate hyperplasia, and diffuse hyperemia of the gland; (2) advanced stage, with high metabolic rate, marked exophthalmos, marked nervous syndrome, marked thyroid enlargement, advanced hyperplasia, diffuse hyperemia, but little if any stored colloid, and (3) the late stage, with high, but sometimes declining metabolic rate, marked nervous syn-

drome; but there is now marked colloid storage, with less hyperemia. The gland is not nodular. Distinct from this picture is a slowly developing type, with increased metabolic rate, but no ocular change, and very frequently associated with nodular thyroids. This Plummer has called hyperfunctioning adenoma. An effort has been made to determine the difference between the two groups of cases, and to sort patients with symptoms from those without. Two groups at the extremes of the metabolic series have been chosen. Group A included patients with enlarged nodular thyroids, with symptoms of hyperthyroidism, but no exophthalmos, no nervous syndrome, with metabolic rate 20 or more above normal. Group B included patients with enlarged nodular thyroids, without hyperthyroid symptomatology and with metabolism rates within 10 points of normal. About 250 thyroids in each series were studied microscopically. Group A cases showed parenchymal cell hypertrophy with some colloid storage. Grossly the glands are: (a) diffuse colloid without new follicle formation, or (b) colloid with new follicle but no capsule formation, or (c) definitely encapsulated areas. These are all of moderate degree. These cases differ in kind and in degree from true exophthalmic goiter. The colloid is passing into the circulation from the parenchymal cells. The parenchymal cells are not under high functional pressure, discharging secretion directly into the vessels. In the new follicle-forming type, we cannot find evidence that this is the essential factor in hyperthyroid symptoms, as even when this picture predominates, there are many areas of colloid absorption by reactivated parenchymal cells. Group B showed no evidence of cell hypertrophy or hyperplasia. The cases could be divided more or less into three groups paralleling those of glands from the hypertrophic series. A few were proliferating adenomas. Disturbance of metabolic rate is the true index of hypothyroidism and hyperthyroidism. Thus the hypertrophic and hyperplastic cells in Group A are responsible for increased metabolic rate, while in Group B there is no substance secreted sufficiently to increase metabolism. One can consider the hypothesis then that symptoms of nonexophthalmic hyperthyroidism are caused by absorption of complete thyroxin secreted in previously stored colloid, but more slowly than in exophthalmic goiter. Stored colloid does contain thyroxin, and the colloid is transmitted from the follicles to the circulation. In true exophthalmic goiter the symptoms may be caused by incompletely elaborated thyroid secretion. This harmonizes with many clinical findings. However, it may be discovered that the disease, true exophthalmic goiter, is primarily a lesion of the nervous system, and that thyroid hyperfunction is a secondary development.—Quoted.

(THYROID) Sexual status in sporadic cretinism (Zur Frage der Sexualität bei sporadischem Kretinismus). Wollenberg (H. W.), Med. Klin. (Berl. & Wien.), 1922, **18**, 144.

Short report of a female cretin (infantile myxedema) who at the age of 8 years could not run or speak properly and who had the growth of about a 2 year old child. She is now 28 years old, 130 cm. high, but with well developed external female characteristics. Menstrual periods have been regular since 18 years of age and are not modified by cessation of treatment with thyroid tablets, which were taken daily for a period of 12 years. She has been pregnant three times since 1919.—A. T. R.

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Endocrinology

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SPECIAL NOTICE

We regret very much the delay in bringing out this number of ENDOCRINOLOGY. This has been occasioned primarily by a severe illness and circumstances arising from the same.

The January number is well along in the process of manufacture, but will not be ready for mailing until February. Announcement of its contents will be found elsewhere.

COMPLETION OF VOLUME VI

This number of ENDOCRINOLOGY completes its sixth volume. The total number of pages is 954, exclusive of the annual index, to be found at the close of this number. This is 126 pages more than contained in Vol. V. and 240 more than in Vol. IV.

During this year there have been published 37 original papers dealing with the various aspects of the endocrine glands. The abstract department has 1622 items, over 40% in addition to the number published last year. The complete cross index to be found in this issue makes all of the material readily accessible for study or for reference.

For those individuals and libraries who bind their journals a Title Page and Table of Contents will be found just preceding the first page of this issue. This is a separate signature and may be removed by the binder and transferred to the beginning of the volume.

May we take this occasion to thank all those who have contributed to the successful year now closed, and to assure you that this cooperation is appreciated. We shall strive during the coming year to be of greater service to you than we have been able to be in the past. On another page you will find the titles of the papers we have in hand for the first number of Volume Seven.

We wish you a Prosperous 1923.

COMING IN THE JANUARY NUMBER

New experimental data on the question of the seat of the endocrine function of the testicle. Alexander Lipschütz, et al., University of Dorpat, Esthonia.

Experimental investigation of the value of various commercial ovarian extracts. Samuel H. Geist, M. D., F. A. C. S., Mt. Sinai Hospital, and Wm. Harris, New York.

A roentgenographic study of the sella turcica in normal children. Murray B. Gordon, M. D., F. A. C. P., and A. L. Loomis Bell, B. S., M. D., Brooklyn.

The epinephrin content of commercial suprarenal "cortex" preparations. Emil J. Baumann, Montefiore Hospital, New York.

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